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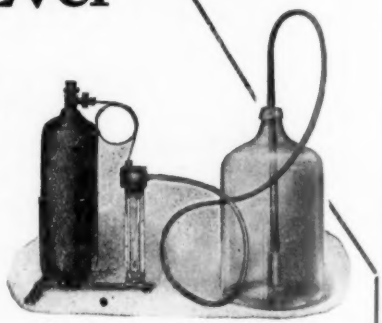

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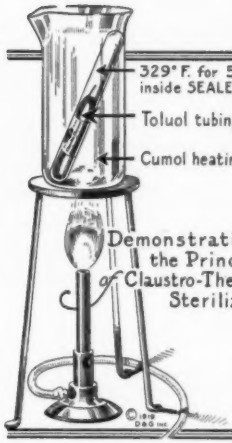
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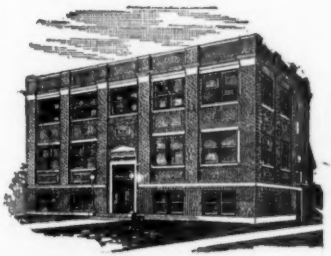

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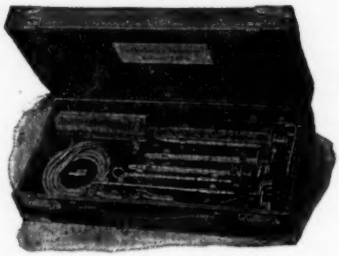

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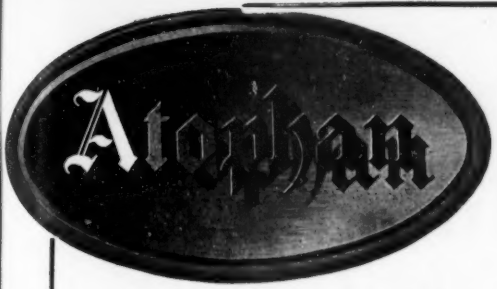

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ORIGINAL ARTICLES

RECENT ADVANCES IN GASTRIC PHYSIOLOGY.[1]

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In the lower animals and in embryos the gastro-intestinal tract is a simple tube from pharynx to anus. The stomach is formed by the bulging and bending of this tube and by the addition of one or more cecal pouches. In a 10-mm. human embryo the stomach is made up of three parts: The expanded lower end of the esophagus, the long tubular antrum (almost indistinguishable from the duodenum) and a small fundus. The end of the esophagus meets the pyloric antrum at the incisura angularis. Later, the fundus grows at the expense of the other parts, so that in the adult the pyloric antrum is comparatively small and the end of the esophagus is represented only by the cardiac antrum and a prolongation along the lesser curvature which forms the gastric canal.[2] (See Fig. 1.) Remnants of the "primitive tube" must then be looked for along the lesser curvature. It is interesting that this region is lined by a mucous membrane very similar to that in the bowel, whereas in other parts of the stomach we find the highly differentiated acid-forming cells.[3]

[1] Read before the American Gastro-enterological Association, Atlantic City, June 9, 1919.

[2] Lewis: Am. Jour. Anat., 1912, xiii, 500. Keith and Jones: Jour. Anat. and Physiol., 1902, xxxvi, 34.

[3] Bensley: Am. Jour. Anat., 1902, ii, 122. Lansdown and Williamson: British Jour. Surg., 1914, ii, 308. Haane: Arch. f. Anat. u. Physiol., Anat. Abth., 1905, 1.

There is considerable evidence for the view that the rhythmicity of the primitive gastro-intestinal tube was graded downward from pharynx to anus much as the rhythmicity of the primitive heart tube is graded from the venous to the aortic end.[4] During its development the heart tube is twisted on itself and develops bulgings in which the future auricles and ventricles are to be. In these regions the muscle is specialized so that it can contract more quickly; it becomes more like striated muscle, and in so doing it loses much of its original rhythmicity.[5] Through all these changes, however, a small strip of primitive highly rhythmic tissue remains, with its venous end still acting as the pacemaker. Similarly in the stomach we shall see that specialization in function has been accom-

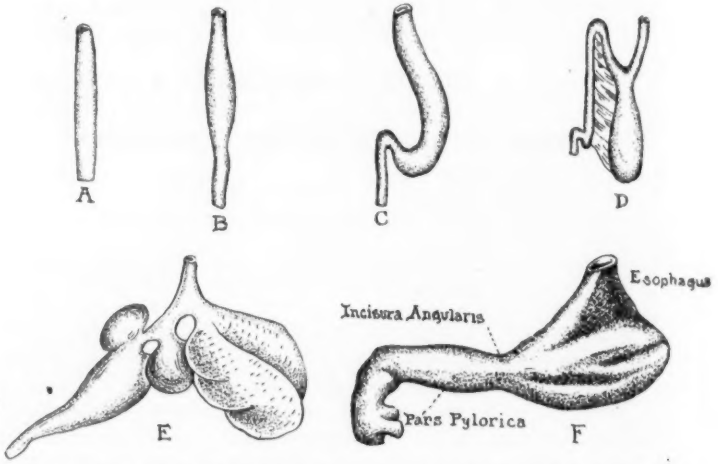

FIG. 1.—To show the development of the stomach. (*a*) Stomach of the pickerel (Nuhn); (*b*) stomach of Proteus anguineus (Nuhn); (*c*) stomach of Scincus ocellatus (Nuhn); (*d*) stomach of the eel (Huntington); (*e*) scheme of the ruminant compound stomach (Nuhn); (*f*) stomach of a 10 mm. human embryo (Lewis).

panied by a specialization in the muscle and a loss in rhythmicity. As we should expect, the most rhythmic muscle is to be found along the lesser curvature with what may perhaps be likened to a pacemaker at the cardia. Although the analogies are close, to avoid confusion it must always be remembered that the functions of heart and stomach are very different. In one the impulse spreads so rapidly that the organ appears to contract as a unit; in the other a series of waves travels slowly over the sac, gently kneading its contents.

[4] Alvarez: Am. Jour. Physiol., 1916, xl, 585.
[5] Gaskell: Schäfer's Text-book of Physiology, London, 1900, ii, 177.

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Differences in rhythmicity were shown by cutting off little strips of muscle from different parts of the stomach and getting them to contract in warm aërated Locke's solution. The segment from the lesser curvature next to the cardia always showed the greatest tendency to rhythmic contraction. Strips from the greater curvature, and particularly from the pyloric antrum, were slow in starting and many would not contract at all. Fig. 2 shows that the rate of contraction was fastest at the cardia and that it decreased progressively to the pylorus. The amplitude of contraction was small near the cardia and along the lesser curvature. It was larger in the pre-antral region and largest in the antrum. These peculiarities were found not only in various animals, but also in the stomach of an executed criminal obtained a few minutes after death. (See Fig. 3.)

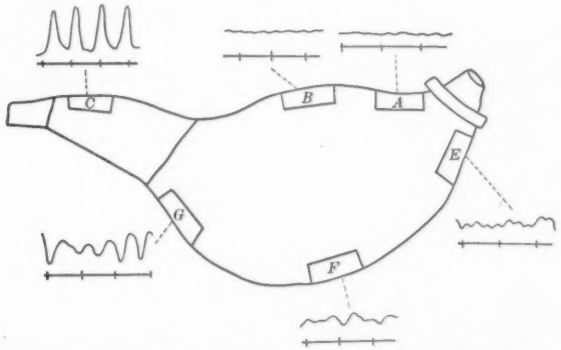

FIG. 2.—A diagram of the cat's stomach to show the location of the principal strips studied and the types of tracing peculiar to the different regions. The time tracing represents thirty-second intervals.

If we watch the human stomach with the fluoroscope the contractions seem to begin on the greater curvature near its middle or a little below. As they approach the antrum they deepen and suddenly their whole character changes. The indention becomes equally deep on the two curvatures, so that the wave may cut the stomach shadow almost in two. It seems to me that these local differences in the peristaltic wave correspond perfectly to the regional peculiarities of tone and amplitude in the muscle through which it must pass. Serial roentgen-ray plates show that the waves do originate near the cardia, but that there they are very shallow.[6] It is probable, then, that the waves which seem to begin in the lower third of the stomach have come as ripples from the highly rhythmic region on the lesser curvature near the cardia.

[6] Groedel: Die Magenbewegung, 1912, p. 68. Dietlen: Ergebnisse d. Physiol., 1913, xiii, 87.

Although the direction of peristalsis may be maintained by or due mainly to the gradient in rhythmicity, other important and closely related gradients can be demonstrated. In the first place the region around the cardia is the most irritable part of the stomach. It also has the shortest latent period.[7] Fig. 4 shows how the latent period is graded from one end of the stomach to the other. The importance of this gradation is shown best in the simple stomach of the frog. There an electric stimulus to the pyloric antrum will show itself as a contraction in thirteen or four-

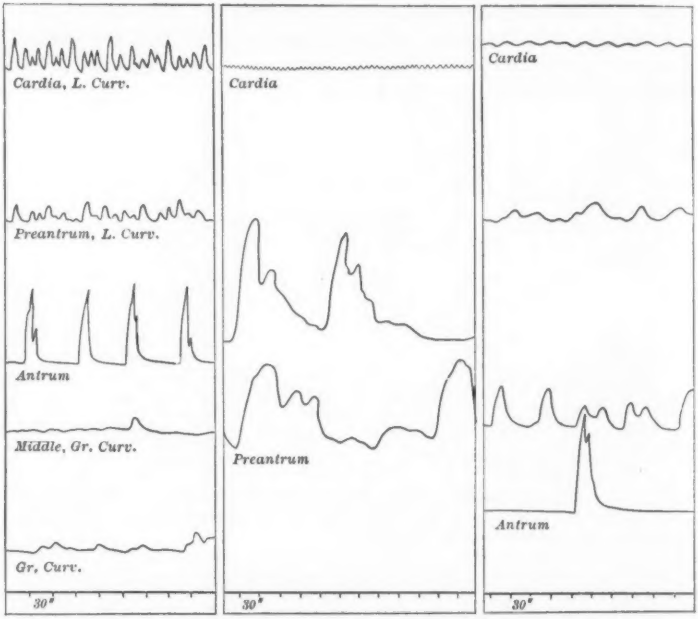

FIG. 3.—Records from five strips from different parts of the dog's stomach; of three strips from the lesser curvature of the human stomach and from four strips from the greater curvature of the human stomach.

teen seconds. Before that time elapses, however, the stimulus spreads to the cardia, where, after eight seconds, it shows itself as a peristaltic wave. This wave gets well down toward the pylorus before any change is visible at the point stimulated. We see then that this mechanism alone could ensure the aboral direction of peristalsis.

The same gradation in the latent period was shown in the excised strips of muscle when they were stimulated in a warm, moist

[7] Alvarez: Am. Jour. Physiol., 1916, xli, 321.

chamber.[8] This study again brought out marked differences in the characteristics of the tissue from different parts of the stomach. The cardiac muscle was very delicate and suffered a great deal from the trauma of excision, handling and stimulation. The antral muscle, on the other hand, was tough and would react well after much trauma. It reacted even better after it had been in the ice-box for forty-eight hours than it did at first. The cardiac muscle often would not react at all after such treatment. The shape of the contraction curve on the smoked drum was different and characteristic for different regions of the stomach. The muscle from the fundus showed a great tendency to remain tonically contracted after stimulation while the antral muscle relaxed promptly. The pyloric antrum seems to be particularly fitted to carry on the active muscular work of the stomach while the fundus serves to

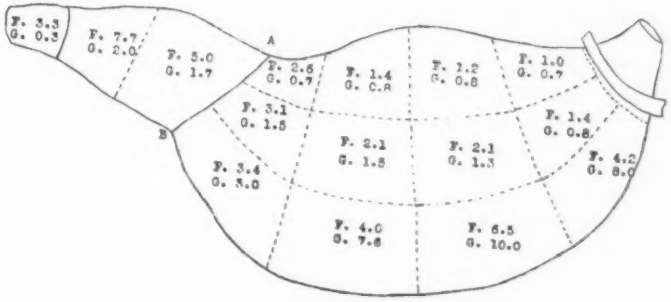

FIG. 4.—Anterior surface of the stomach of the cat, showing the average latent periods after faradic and galvanic stimulation in different regions. The figures indicate seconds. *A B* is the dividing line between the pars pylorica and the body of the stomach. The other unbroken line represents the pylorus.

maintain a steady tonic pressure on the contents. The muscle from the antrum has a color different from that in the rest of the stomach: it is redder and tough like a gizzard. The muscle in the pacemaking region is the softest to the touch.

UNDERLYING METABOLIC DIFFERENCES. As one after another of these regional differences came to light it seemed to me that there must be underneath them all differences in chemical structure and in the rate of metabolism. The first work on this problem was done on the small intestine.[9] Little difficulty was encountered there in demonstrating a gradient of CO_2 production in the muscle from the duodenum to the ileum. Remarkably parallel to this gradient was a gradient of catalase content. Catalase is the ferment which liberates oxygen from hydrogen peroxide. A great

[8] Alvarez: Am. Jour. Physiol., 1917, xlii, 422, 435.
[9] Alvarez and Starkweather: Ibid., 1918, xlvi, 186.

deal of work has been done which indicates that in some way this substance is involved in the process of tissue oxidation. Tissues with high rates of oxidation usually have more catalase per unit of weight than have tissues with slower rates of oxidation. It seems most likely, then, that the gradient of catalase content which Miss Starkweather and I have found in the wall of the stomach represents a gradient of metabolic activity.[10] This gradient corresponds quite well to the gradient of rhythmicity already established. Furthermore, just as there is a sudden change from a low rhythmic rate in the antrum to a fast rate in the duodenum, so we find an abrupt rise in the catalase content as we cross the pyloric line.

So far very little work has been done on the anatomical side of the problem. Keith[11] has found nodal tissue in the highly rhythmic area on the lesser curvature near the cardia. Openchowski[12] found peculiar ganglion cells around the cardia different from those in Auerbach's plexus. Schütz[13] and L. R. Müller[14] have made similar observations. Although big histological differences have been found in striated muscles and in the heart, very little attention has been paid to this point in the stomach and intestine. McGill[15] found an embryonic type of smooth muscle persisting in some parts of the tract, but unfortunately does not remember just where these islands were.

More work should be done also on the pylorus. It is not generally known that there is a fairly complete connective-tissue barrier between the muscle of the antrum and the duodenum. Ordinarily there are only a few bundles from the longitudinal coat which pass over.[16] This explains the fact that the gastric waves do not run over on to the duodenum. Graphic records show that some influence may pass over to start peristaltic rushes in the bowel, but the deep waves, visible to the unaided eye, certainly stop at the barrier.

Clinical Applications. After years of experiment it has been established that the stomach can perform its functions quite satisfactorily after section of all extrinsic nerves.[17] Now, we see that these functions are probably dependent upon graded differences in rhythmicity, irritability, latent period and metabolism in the local neuromusculatory apparatus. If this is true, then any changes in these gradients must influence the peristalsis and the emptying time of the stomach. Such changes have been found in sick animals. In distempered dogs and snuffling cats the gradients of

[10] Alvarez and Starkweather: Am. Jour. Physiol., 1918, xlvii, 60.
[11] Lancet, 1915, ii, 371.
[12] Deutsch. med. Wchnschr., 1889, xv, 717; Zentralbl. f. Physiol., 1889, iii, 2.
[13] Arch. f. Verdauungskr., 1908, xiv, 242.
[14] Arch. f. klin. Med., 1911, ci, 421.
[15] Am. Jour. Anat., 1909, ix, 528.
[16] Cunningham: Tr. Roy. Soc. Edinburgh, 1905–07, xlv, 9. Brinton: Diseases of the Stomach, London, 1859, p. 268.
[17] Cannon: Am. Jour. Physiol., 1906, xvii, 429.

latent period and metabolism were often reversed and practically always made irregular and less steep. This was due probably to the fact that the muscle at the cardia is so much more sensitive to adverse conditions and probably to disease toxins than is the pyloric muscle. Similar upsets were observed in the intestinal gradients in these sick animals.

The gradient might be reversed also by an irritating lesion, such as an ulcer near the pylorus, which could raise the metabolic rate in the surrounding muscle above that near the cardia. Such a reversal would probably give rise to the anastalsis which is seen sometimes with the roentgen rays.

A number of surgeons have commented on the fact that a V-shaped excision of an ulcer on the lesser curvature is likely to interfere with the emptying of the stomach while a sleeve resection usually gives a much better result.[18] We can probably explain that now in the following way: Ordinarily the wave originating at the cardia has to travel faster along the greater curvature than along the lesser curvature because the greater is longer. Apparently both sides of the wave must reach the pylorus at the same time in order to secure good emptying. Now, time and time again while watching the human stomach under the screen I have seen the two sides of the wave reach the antrum unevenly, so that they met not at the pylorus but at a point on one side or the other. Sometimes this was due to an ulcer on the lesser curvature, and at other times I could not see what had interfered with the conduction. Sometimes the arrival of part of the wave at the pylorus seemed to block the other part of it still advancing along the greater curvature. It seems to me probable that such differences in conduction would be still more exaggerated after an operation which shortens the lesser curvature. Under these circumstances one side of the wave might reach the pylorus long before the other. Theoretically a sleeve should be removed with a longer side on the greater curvature than on the lesser.

While watching gastric peristalsis in the rabbit and also in man it has often seemed to me that there must be a wave of excitation travelling ahead of the visible contraction. Owing to its greater irritability and shorter latent period the pyloric ring responds to the excitation a little ahead of time. The resulting contraction blocks the advancing peristaltic wave and keeps it from putting any pressure on the sphincter. This may explain why some stomachs do not empty well in spite of good peristalsis and a patent pylorus. Time and again in cats I have watched a similar mechanism at work at the ileocecal ring causing it to contract firmly in the face of advancing colonic waves. The contraction ring thus

[18] Mayo: Jour. Am. Med. Assn., 1915, lxv, 1073. Stewart and Barber: Ann. Surg., 1916, lxiv, 527.

formed served to block these waves before they could put much pressure on the sphincter.

While peeling off the strips of muscle it was found that the submucosa was quite deficient along the lesser curvature from the cardia to the antrum. The mucosa is fastened to the muscle there much as the skin is to the palmar fascia of the hand. In the rest of the stomach, and particularly in the antrum, the strips could be peeled off easily. These differences may have some influence on the spread of carcinoma and on the penetration of ulcer.

It is an interesting observation that in animals the region corresponding to the duodenal cap has a poor rhythmicity. Excised segments put into warm oxygenated Locke's solution often do not contract at all, and when they do they generally show an irregular rhythm with small amplitude. This may be due partly to the peculiar festoon-like arrangement of the muscle fibers in this region. As would be expected, this comparatively inactive segment, situated as it is between two strong and active ones, tends to remain filled with food for long periods of time.

It is a well-known fact that carcinoma very rarely originates in the duodenum, and when it begins in the stomach it will not spread across the pyloric line. It seems probable now that this is due to a difference in metabolic rate on the two sides of that line. Estimations of the catalase content of the mucous membrane from different parts of the digestive tract showed that the lowest figures are to be obtained in the pyloric antrum and the highest in the duodenum.[19] (Fig. 5). Now, Child[20] has shown, with simple forms of life, that the embryonic, undifferentiated and rapidly growing cell loses its capacity for growth as it fills up with the comparatively stable structural substances which are acquired during differentiation and specialization. This process leads to senescence and death. After the metabolism has become greatly slowed these cells may suddenly begin to use up this metaplasm; they dedifferentiate and reacquire the faculty of growth. Goodpasture[21] has recently pointed out how this mechanism, so useful in the rejuvenation of simple forms of life, can threaten the existence of the higher forms. It may be, then, that that part of the gastric mucous membrane with the lowest metabolic rate is, as it were, most senile and therefore most subject to cancer. Tumors originating there cannot spread into a mucous membrane which is kept young by its high metabolic rate.

One other thing might be mentioned, and that is the apparent uselessness of gastric faradism as a therapeutic measure. I found it impossible sometimes to get contraction of the gastric muscle when strong currents were applied directly to the serous coat. This was observed not only on animals opened under an anesthetic,

[19] Alvarez and Starkweather: Am. Jour. Physiol., 1918, xlvii, 67.
[20] Senescence and Rejuvenescence, Chicago, 1915.
[21] Jour. Med. Res., 1918, xxxviii, 127.

but also at operations on men and women. Meltzer[22] found, many years ago, that it was almost impossible to stimulate the muscle through the mucosa. Even when the current gets through there is no reason to hope that it will act so appropriately as to restore the downward gradients when they have been altered by disease.

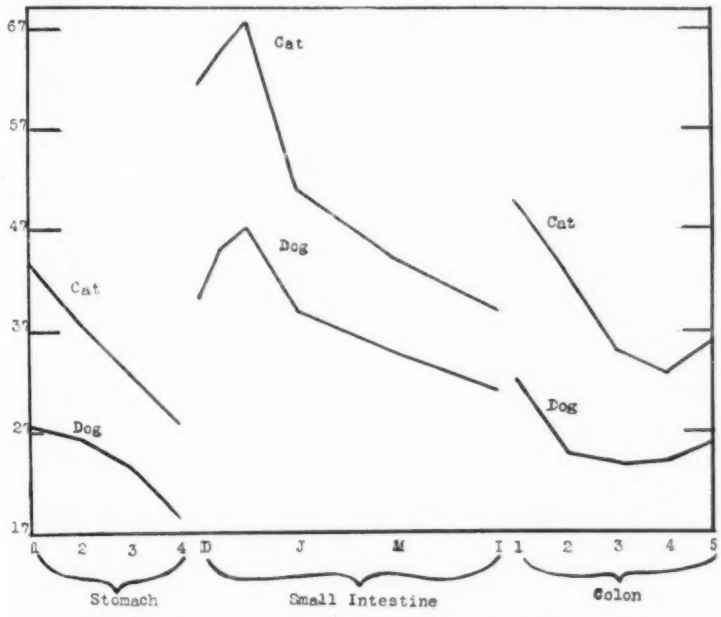

FIG. 5.—Shows the gradation in catalase content of the mucosa in different regions. The ordinates represent cubic centimeters of oxygen liberated in fifteen minutes by 0.2 gram of tissue.

SUMMARY. The gastro-intestinal tube may originally have been constructed so that the rhythmicity of any one segment varied inversely as the distance from the pharynx.

The stomach has been evolved from this simple tube much as the heart has been enlarged and specialized. The remnants of the primitive tube are to be looked for along the lesser curvature.

A highly rhythmic area has been found on the lesser curvature near the cardia.

Strips of muscle excised from different parts of the gastric wall can be made to beat rhythmically in warm, aërated Locke's solution. Speaking roughly, the rate of contraction varies inversely as the distance from the cardia.

[22] New York Med. Jour., 1895, lxi, 746.

Differences in the depth of the waves as they sweep over the stomach can be explained by differences in tone and amplitude of contraction of the muscle in different parts of the organ.

There is a gradient of irritability from cardia to pylorus. The latent period is shortest near the cardia and longest in the pyloric antrum.

The muscle in the pars pylorica appears to be quite different from that in the rest of the stomach. It is especially fitted to do the hard work of that organ.

The pyloric ring is more irritable and has a shorter latent period than that of the pyloric antrum. This may have considerable bearing on the problems of poor gastric emptying in ulcer.

The duodenum is much more irritable than the antrum and its rhythmic rate is much higher.

The muscle on the lesser curvature near the cardia is very sensitive to trauma and to adverse conditions which seem to have no effect on the muscle from the antrum. This difference may account for the fact that the normal downward gradients of rhythmicity and latent period were altered and even reversed in sick animals.

Evidence is presented which suggests strongly that there is a gradient of metabolism underlying and perhaps giving rise to the gradients of irritability, latent period and rhythmicity which, it is believed, determine the direction of peristalsis. The metabolic gradient is often found reversed in sick animals which are refusing food.

There appears also to be gradient of metabolism in the mucous membrane of the stomach. The lowest values in the whole digestive tract are found in the antrum. It is shown how this may explain the high incidence of cancer in that region and the inability of the tumors to cross over into the duodenum, where there is a very high metabolic rate.

An explanation is given for the fact that a sleeve resection gives a better functional result in ulcer of the lesser curvature than a V excision.

PERSISTENT EOSINOPHILIA WITH HYPERLEUKOCYTOSIS AND SPLENOMEGALY.[1]

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As the basis for a discussion of eosinophilia I wish to review a case which seems to be unique in medical literature: eosinophilic hyperleukocytosis associated with marked splenomegaly and mod-

[1] Presented before the Association of American Physicians, June 16, 1919, Atlantic City, N. J.

erate glandular enlargement. This case suggests a consideration of (1) the origin and function of the eosinophils, (2) the clinical incidence of eosinophilia, (3) the occurrence of eosinophilia with hyperleukocytosis, and (4) the possibility of the existence of an actual eosinophilic leukemia, apparently following splenectomy in a case of eosinophilic hyperleukocytosis.

CASE 81201.—*F. H., male, aged thirty-one years. Marked splenomegaly. Slight enlargement of superficial lymphatic glands. Leukocytosis* 21,800 *before splenectomy, with an eosinophilia of* 73.6 *per cent. Splenectomy July* 15, 1914. *Weight of spleen* 2110 *grams. Macroscopic appearance of spleen similar to that of myelogenous leukemia. Rapid increase of leukocyte count to* 97,200 *and later to* 211,000, *eosinophilia from* 79 *to* 90.7 *per cent. Good general condition for period of four years following splenectomy. Death January* 19, 1919, *of empyema following pneumonia. Necropsy: Enormous numbers of eosinophilic polymorphonuclears in all hemopoietic organs. Eosinophilic myelocytes numerous in lymph glands, spleen and bone-marrow. Obliterative pericarditis and fibrous perihepatitis.*

March 11, 1913, a man, aged thirty-one years, with generalized anasarca and moderate anemia, presented himself for examination. His family history was negative. He had had a continuous fever, with the characteristics of typhoid fever, eight years previously, and this had been followed by pneumonia. Convalescence from this severe illness was protracted and the patient had not since that time entirely regained his former strength. Eighteen months before the examination he developed moderate dyspnea and a cough; he had an occasional attack of vomiting and some wheezing, but did not have a typical paroxysmal asthma. Thirteen months before, he had been much annoyed by a severe recurrent pain in the left thoracic region; this, in the light of later findings, may have been due either to a pericarditis, a pleurisy or to a perisplenitis. Ten months before examination a transitory edema of the legs and face developed, which would disappear during the night. Five weeks previous to examination the patient became quite ill with cough, shortness of breath and wheezing, without chill or fever. He could not work, but was not confined to bed. Three weeks before examination he began to suffer from a moderately severe pain at the right costal margin, associated with vomiting and questionable jaundice. One week before examination a generalized edema developed and became progressively worse.

The general physical examination showed a marked superficial edema of the legs and body up to the level of the arm-pits. The scrotum was edematous; evidence of ascites was present, the liver and spleen were enlarged and the axillary glands were easily palpable. There was no definite evidence of lues and the Wassermann test was negative. There was no indication of nephritis. The acute condition at that time seemed to be due either to a myocardial insufficiency or a cirrhosis of the liver.

The most interesting finding, however, was the presence of eosinophilia of 66.3 per cent. (see Table). The leukocyte count at the time of the first examination in March, 1913, was 15,400; the total lymphocyte count was 19.3 per cent. while the polymorphonuclear count was only 13 per cent. The anemia itself was of a secondary type, with a red cell count of 3,620,000 and a hemoglobin of 69 per cent. On account of the extremely high eosinophilia a very careful search for parasites was made. The stools were repeatedly negative and a microscopic examination of skeletal muscle was negative.

BLOOD COUNTS (CASE 81,201, F. H.).

Date	Mar. 11, 1913.	Dec. 16, 1913.	July 14, 1914.	Splenectomy, July 15, 1914	Aug. 5, 1914.	Nov. 24, 1914.	May 25, 1915.	Dec. 5, 1916.	May 15, 1917.	Oct. 10, 1917.	Nov. 26, 1918.
Hemoglobin	69	80	75		68	85	70	69	52	58	50
Red blood cells (millions)	3.62	4.16	3.86		4.02	4.60	3.56	4.25	3.48	3.62	2.72
White blood cells	15,400	15,400	21,800		97,200	133,000	208,000	103,000	211,000	135,000	81,800
Small lymphocytes	18.3	16.0	9.6		6.8	11.3	5.0	9.0	3.7	5.3	5.0
Large lymphocytes	1.0	4.8	6.0		1.2	1.3	4.2	0.3	1.0	2.0	1.7
Polymorphonuclears	13.0	19.4	9.8		12.4	10.0	6.8	6.7	4.3	5.7	7.0
Eosinophils	66.3	57.6	73.6		79.0	75.0	83.4	83.0	90.7	87.0	84.0
Basophils	1.3	2.2	1.0		0.6	2.3	0.4	..	0.3	..	0.7
Neutral myelocyts	..	..	..		..	..	..	0.3			
Eosinophile myelocytes	..	..	..		..	..	0.2	..	..	..	0.7
Normoblasts	..	..	..		..	..	1.	1.	..	..	1.

A lymph gland removed from the axilla for microscopic examination showed a moderate inflammatory reaction. The germ centers were intact; a marked endothelial hyperplasia was present. Eosinophilic polymorphonuclear leukocytes were quite numerous and a few scattered eosinophilic myelocytes were to be found.

The patient was placed at absolute rest in bed on a milk diet; his edema practically disappeared within ten days. The spleen was then easily outlined and was found to extend to the navel and to the level of the left iliac spine. Two months later the patient was able to do light work. During the summer and fall of 1913 he worked moderately hard and quite regularly. In June, 1914, more than one year after the original examination, the patient's general condition was fairly good. His anemia, however, was quite definite; the red cell count was 3,500,000, the eosinophile percentage was 75.4, while the total leukocyte count was 13,800.

In view of the persistence of a chronic anemia of the secondary type and the presence of a marked splenomegaly, splenectomy was decided on. The operation was performed on July 15, 1914, by W. J. Mayo. The spleen was very large, measuring approximately ten inches by 12 inches, and weighing 2110 grams. Extensive perisplenitis was present and the organ was almost completely adherent to the vault of the diaphragm, to the wall of the stomach and to the parietal peritoneum. Macroscopically it had the appearance of the

spleen in myeloid leukemia. The liver, especially the left lobe, was very large. A small amount of abdominal fluid was present. The gall-bladder was distended, but gall-stones were not palpable.

Splenectomy was followed by a gradual and steady improvement, especially with respect to the patient's strength and general condition. Within one month after splenectomy, however; the leukocytes had risen from 21,800 to 97,200, 79 per cent. of which were eosinophils. During the fall of 1914 the patient felt better than for seven or eight years. His weight was 159 pounds and he was able to do light work. The liver remained enlarged and in November, 1914, it extended three finger-breadths below the costal margin. The superficial glands in the neck and axilla were easily palpable. During 1915 the patient's general condition was quite satisfactory, aside from slight shortness of breath on exertion. During the winter of 1916 there was a slight increase in the size of the liver and a superficial edema was occasionally present, but by summer the patient was so improved that he was able to do regular farm work. A pruritus of indeterminate type developed; this may have been an expression of the patient's chronic toxemia. In 1917 the patient's general condition was quite satisfactory except for occasional attacks of pruritus and of moderate dyspnea and edema. October 10, 1917, the leukocytes numbered 135,000, 87 per cent. of which were eosinophils. The patient continued to be in fairly good health until October, 1918, at which time a gradually increasing weakness, dyspnea and cough developed, later associated with an acute illness, which probably was pneumonia, as our examination in November, 1918, revealed evidences of unresolved pneumonia, and a roentgen-ray examination of the chest showed an infiltration in the region of the right middle lobe, together with a considerable enlargement of the cardiac shadow. The patient was anemic, the hemoglobin being 50 per cent. and the red cells 2,720,000. The patient was advised to have hospital care and observation, but this was refused; one month later he returned in a very bad condition. There was then evidence of fluid in the right pleural cavity. A catheter was inserted through a cannula and 1300 c.c. of yellow pus were aspirated. A culture showed pneumococci. Through an oversight a cellular and chemical study of the pus was not made. The pleural cavity was treated with Dakin solution. The patient's general condition was not satisfactory after the development of empyema, and on January 18, 1919, his temperature rose rather suddenly to 102°; he died January 19, 1919, probably as the direct result of bronchopneumonia.

Cytology of Blood Smears. A study of the blood smears revealed that almost all the eosinophils were of mature type and differed only slightly from the eosinophilic polymorphonuclears which are ordinarily found in the blood-stream. These cells were somewhat larger than usual and the number of nuclear lobes was increased. Many

cells had three lobes. The protoplasm seemed to be basophilic rather than neutrophilic and a considerable vacuolation was present while a few cells were ruptured. Certain eosinophils were to be seen in which a few small basophilic granules were present and an occasional eosinophil had the appearance of a transitional cell or metamyelocyte with a horseshoe nucleus. Rarely, however, was it possible to discover a true eosinophilic myelocyte in the blood smears (Fig. 1, *a*).

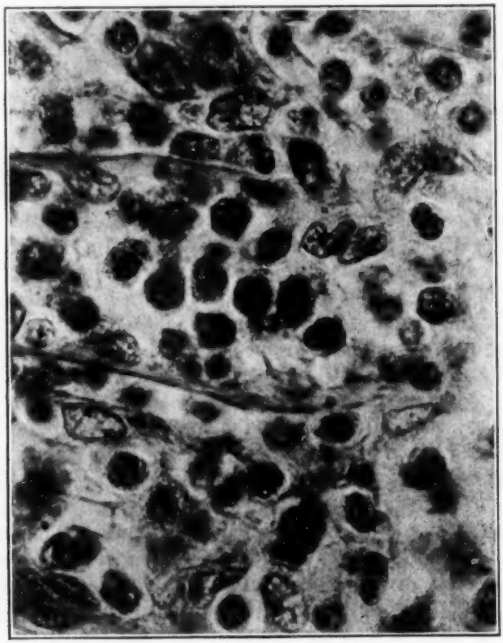

FIG. 2.—Microphotograph of spleen, showing eosinophilic polymorphonuclear leukocytes and myelocytes. They are not so plain in the spleen as they are in the lymph gland (Fig. 5), due to poor fixation.

Examination of the Spleen Removed at Operation July 15, 1914.* The spleen, weighing 2110 grams, was approximately ten by twelve inches. The Malpighian bodies were intact though not numerous. Cellular hyperplasia was marked, eosinophilic polymorphonuclears were very numerous and a few eosinophilic and neutrophilic myelocytes were seen. The increase in the amount of fibrous tissue was only slight (Fig. 1). The myelocytes were much less numerous in

* Examination of tissues was made by A. C. Broders.

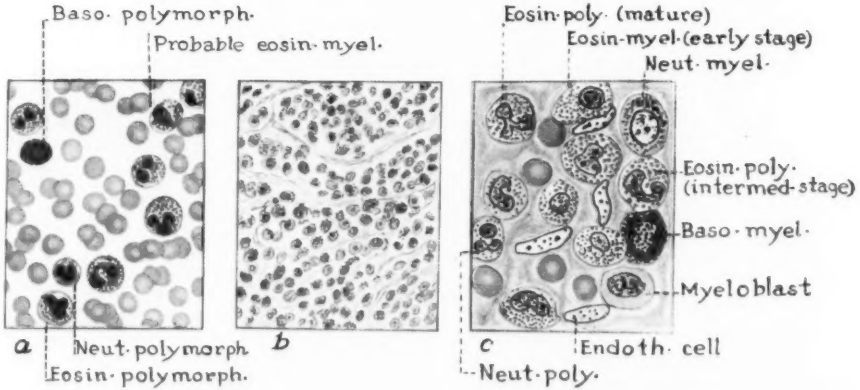

Fig. 1.—Drawings of Actual Fields to Show Eosinophiles.

a. Eosinophiles in the blood stream, observed with 10 × ocular and ½ immersion oil objective.

b. Bone-marrow cells showing remarkable predominance of eosinophilic myelocytes, ⅙ objective, 10 × ocular.

c. Bone-marrow under ½ immersion oil objective and 10 × ocular.

the spleen, which was removed in 1914, than they were in the glands removed at necropsy four and one-half years later.

Examination of the Bone-marrow (*Postmortem January* 19, 1919.) The bone-marrow was hyperplastic and contained great numbers of eosinophilic polymorphonuclear leukocytes; the majority of them were in a well-developed stage while a few were apparently of intermediate type. Eosinophilic myelocytes were present in the proportion of 3 to 10 in favor of eosinophilic polymorphonuclears. An occasional neutrophilic polymorphonuclear and, very rarely, a basophilic myelocyte could be found. The erythrogenic function of the bone-marrow seemed to be almost in complete abeyance (Figs. 1*b* and *c*, and 3 and 4).

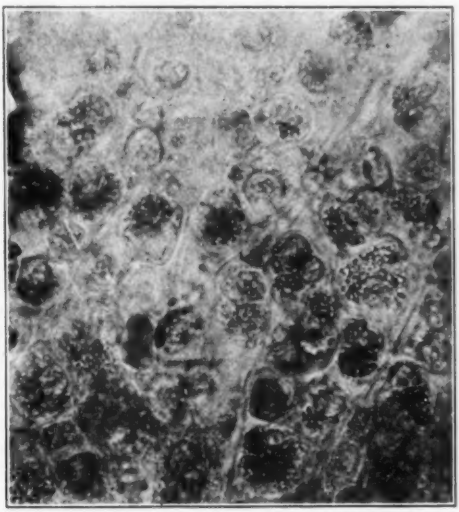

FIG. 3.—Microphotograph of bone marrow, showing numerous eosinophilic polymorphonuclear leukocytes and a few eosinophilic myelocytes. The coarse granules, often clumped at one side of the cell, are prominent. 10X ocular, $\frac{1}{12}$ objective, Jenner stain.

*Examination of the Lymph Gland from the Region of the Head of the Pancreas.** The gland was about 3 cm. in diameter. The germ centers were intact. Eosinophilic polymorphonuclears were very numerous. A few scattered eosinophilic myelocytes and neutrophilic myelocytes were found. The eosinophilic myelocytes occurred in the proportion of 1 to 10 in favor of the eosinophilic polymorphonuclears. The eosinophilic polymorphonuclears showed chiefly fully developed forms and occasionally intermediate forms. The

*Examination of tissues was made by A. C. Broders.

eosinophilic polymorphonuclears were almost as numerous as the lymphocytes (Fig. 5).

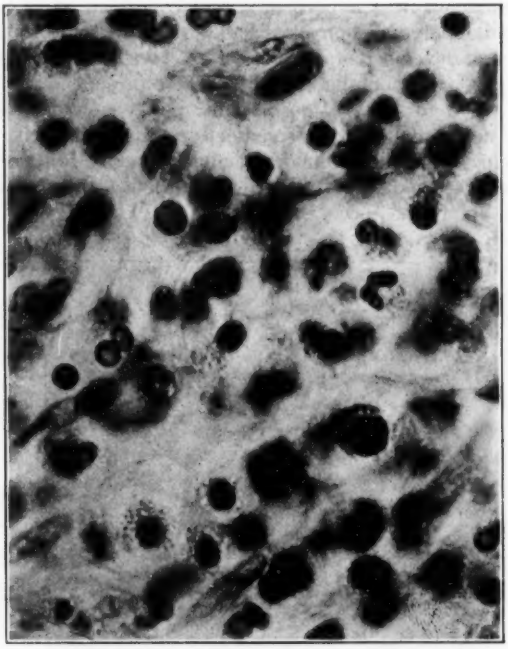

FIG. 4.—Microphotograph of bone-marrow, showing eosinophilic myelocytes and polymorphonuclear leukocytes.

Anatomic Diagnosis. Right bronchopneumonia; right fibrous pleuritis; obliterative pericarditis; fibrous perihepatitis; cirrhosis of the liver; general lymphoid hyperplasia. The obliterative pericarditis and the fibrous perihepatitis were probably of long standing and much of the symptomatology during the last six years of the patient's life could be attributed to cardiac and hepatic disease. While these latter pathological conditions were apparently of a chronic nature the cirrhosis of the liver was of mild grade and of mixed type, but a generalized fibrous peritonitis, commonly seen in Pick's or Concato's disease, was not present.

DISCUSSION.

1. *The Origin and Function of the Eosinophils.* Most hematologists subscribe to the heteroplastic theory of the formation of granular cells, at the same time admitting the occurrence of

mitosis and the homoplastic origin of a certain number of these cells. They agree that eosinophilic polymorphonuclear leukocytes develop chiefly from undifferentiated mononuclear cells within the bone-marrow, and in smaller numbers within certain special tissues of the organism, particularly lymphoid tissue. Whether this development is a direct transformation from lymphocytes or is the result of maturation from metastatic bone-marrow tissue is undecided. In the case herewith reported the presence of eosinophilic myelocytes and immature forms of eosinophilic polymorphonuclears in the spleen and lymph glands indicates quite clearly

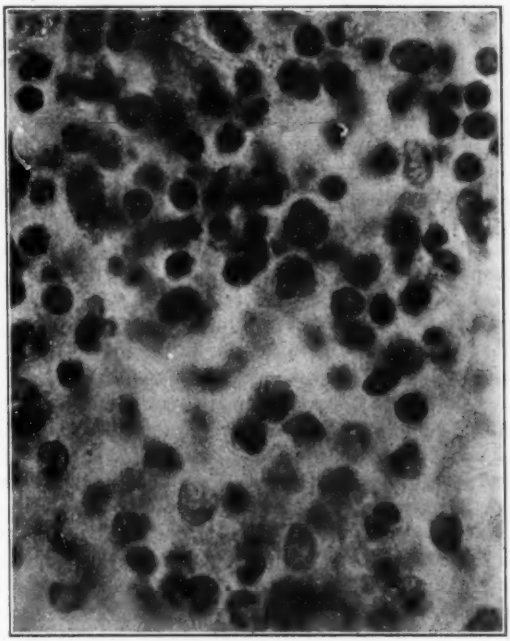

FIG. 5.—Microphotograph of large lymph gland near the head of the pancreas, showing numerous eosinophilic polymorphonuclear leukocytes and a few eosinophilic myelocytes.

either a normal or a perverted production of eosinophils within these organs. There is no conclusive evidence in favor of the theory of the direct transformation of neutrophilic polymorphonuclears into eosinophils either in the blood-stream or in the general tissues. The theory of the origin of eosinophilic granules from hemoglobin or its dissociation products is strongly advocated by Weidenreich. The recent work of Downey shows that in the bone-marrow of the adult guinea-pig eosinophilic granules are differen-

tiated gradually from a basophilic protoplasm and that their progressive evolution is marked by complex changes in staining reactions, size and shape, and also that there is a direct transformation from basophilic to oxyphilic granules. The complex evolution of the granules indicates that they are true endogenous formations. The granules of eosinophils even in the younger cells and before they become clearly oxyphilic can be differentiated from the granules of mast-cells by their size, shape and staining characteristics. Downey explains that there need be no conflict between his own conclusions concerning the endogenous origin of eosinophile granules in the bone-marrow and Weidenreich's demonstration of an exogenous origin as a result of phagocytic activity. This can be explained on the basis of Gütig's theory that two types of eosinophils exist and that, morphologically, they are distinguishable.

Very few facts concerning the function of eosinophils are known. Complete withdrawal of food is followed by a decrease of eosinophils in the peripheral circulation. There is a relationship between nutrition and the production and circulation of eosinophils and disturbances of nutrition affect the multiplication of eosinophils more readily than that of the finely granular leukocytes (Opie). Schwarz believes that there are indications of a very close relationship between eosinophils and intestinal secretion and that possibly these cells may convey a hormone which is important for proper cellular activity in the intestine. Falta and his co-workers call attention to the fact that pilocarpin and pituitrin, substances which raise the tonus of the autonomic nervous system, also produce eosinophilia.

Lepsky concludes that eosinophilia is, in some measure, a reaction of the organism against the penetration of foreign proteins. Weinberg and Séguin, in 1915, confirmed the work of Mesnil and others by demonstrating that eosinophils possess important phagocytic properties with respect to both bacteria and cells; they also showed by the use of hydatid fluid that eosinophils are well adapted to the absorption of toxic products. In their experiments those eosinophils which had absorbed toxic material lost their phagocytic properties while these properties were retained by the neutrophilic and mononuclear cells and the hydatid liquid itself lost its antigenic power. Fiessinger recently has shown that there is a definite antitoxic leukocytic reaction and defense against the foreign proteins formed in war wounds as the result of infection and the destruction of tissue and that eosinophils are concerned in the mechanism of this defense. All of these observations lead to the conclusion that eosinophils may play an important role in the maintenance of immunity.

2. *The Clinical Incidence of Eosinophilia.* Eosinophilia has been described in association with many conditions, although in most of them the percentage is neither high nor persistent. A low grade of eosinophilia is found in some cases of scarlet fever, neurasthenia

and polycythemia. A constant slight relative and marked absolute eosinophilia is present in myelogenous leukemia. Eosinophilia also is associated with the presence of parasites and its occurrence in asthma and in certain cutaneous diseases is well established. The most marked eosinophilias which I have been able to find reported in medical literature have occurred in cases of trichinosis, in which the eosinophilia is transient, of lymphadenoma, especially associated with cutaneous lesions and occasionally in cases of carcinoma and sarcoma. Reports of instances in which the eosinophils have even temporarily reached 25 per cent. or more are exceedingly rare. I have had under observation a patient (Case 104259) with Hodgkin's disease who had an eosinophilia of 33.3 per cent. with a leukocyte count of 12,000. The diagnosis was made after the excision of a gland for microscopic examination. No reason for the marked eosinophilia could be discovered. Aubertin and Girous describe a cardiac case with cyanosis and frequent attacks of decompensation in which a persistent and very high eosinophilia was present. The leukocyte count varied from 6900 to 13,500 and the eosinophils from 57 to 68.25 per cent. Dunger reports a case of probable carcinoma of the colon in which the leukocyte count was 35,330, 60 per cent. of which were eosinophils. Sibley reports an eosinophilia of 39.6 per cent. and a leukocyte count of 28,150 in a case of lymphadenoma associated with cutaneous lesions.

In none of these cases was a markedly enlarged spleen present; in only one instance was the eosinophilia persistent.

3. *The Occurrence of Eosinophilia with Hyperleukocytosis.* After a careful study of the literature only three instances of eosinophilia associated with hyperleukocytosis have been found. Glanzmann describes a case of lymphadenoma as "lymphatic endotheliomatosis," in which the leukocyte count varied from 12,000 to 183,000 and the eosinophiles from 4 to 33.6 per cent. Rheinbach reports a lymphosarcoma of the cervical region, with a leukocytosis of 120,000 and an eosinophilia of 48.28 per cent. The leukocytosis was transient and the eosinophilia fluctuating in these 2 cases. Stillman, in 1912, reported to the New York Academy of Medicine a case of persistent eosinophilia with hyperleukocytosis and splenomegaly. The features of Stillman's case conform closely to those of the case herewith reported, and it is the only similar case that I found in the literature. The leukocyte count varied from 118,000 to 165,000 and the eosinophiles from 85.8 per cent. to 91 per cent. The spleen was slightly enlarged and the lymph nodes were palpable. The patient was under observation for a short time only and his subsequent record is unknown.

4. *The Possibility of the Existence of an Actual Eosinophilic Leukemia.* Our knowledge of eosinophilia in general strongly favors the conclusion that an eosinophilic hyperleukocytosis is not a true

leukemia. The occurrence of eosinophilia has so far been most satisfactorily explained on the basis of the chemotactic theory. In cases of a very chronic type of toxemia or infection it is possible that certain poisons which are effective throughout the entire organism for years may induce a persistent eosinophilia of almost any degree. It has been repeatedly demonstrated that some substances may call forth a local eosinophilia which will have no recognizable effect on the blood count. When the process is more extensive and the chemical irritant affects larger parts of the organism or possibly when a different form of toxin is circulating the demand for increasing numbers of eosinophils, as well as the toxin itself, may react as a physiological stimulant to the production of eosinophils in the bone-marrow and in other hemopoietic structures. A perversion of these tissues may be the result.

In the case which has been reviewed those conditions which may be said to argue in favor of the existence of a true eosinophilic leukemia following splenectomy are as follows: (*a*) The persistently high leukocyte count, (*b*) the marked splenomegaly, (*c*) the general glandular hyperplasia, (*d*) the gross appearance of the glands, spleen, and bone-marrow, (*e*) the occurrence of a small percentage of immature cells and an occasional myelocyte in the blood smears, and (*f*) the presence of active hyperplasia in glands, spleen and bone-marrow, together with the presence in these tissues of numerous eosinophilic myelocytes.

The facts which constitute the evidence against the existence of an actual leukemia are: (*a*) The marked predominance of mature and almost mature eosinophils in the blood-stream and in the hemopoietic system, (*b*) the postmortem demonstration of an obliterative endocarditis, perihepatitis and hepatic cirrhosis, which would account for a greater part of the symptomatology during the entire course of the disease and would indicate the probable presence of a chronic toxemia, (*c*) the absence of hyperleukocytosis before splenectomy, (*d*) the long duration of the disease, approximately seven years and (*e*) the absence of the typical microscopic characteristics of leukemia.

While not entirely discarding the view that an eosinophilic leukemia may have been present at least after splenectomy, I am inclined to regard the case as an instance of eosinophilic hyperleukocytosis, the blood picture of which was remarkably altered by splenectomy. This permanent increase of the leukocytes following splenectomy for a period of four and one-half years considered in connection with the occurrence of a more or less constant eosinophilia after splenectomy for various other conditions, may be indicative of some special function of the spleen with respect to eosinophilic cells or with respect to the toxins which eosinophilic cells are capable of absorbing.

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MEDICAL ASPECTS OF WOUNDS OF THE CHEST IN WAR.[1]

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Introduction. The operative treatment of wounds of the chest as of wounds of other parts of the body is a duty of the surgeon requiring great technical skill, good judgment and mastery of the fundamental principles of surgery.

Chest surgery differs, however, in two important respects from most other classes of war surgery: (1) its field has been much enlarged during the war, and (2) some of the questions which arise in connection with chest cases are of a kind with which the physician is more familiar than the surgeon.

[1] Read in part before the Association of American Physicians June 17, 1919. Service with the Harvard Unit at 22 General Hospital of the British Expeditionary Forces in 1916, 1917 and 1918 and attached to Casualty Clearing Stations at various times in 1917 and 1918.

For example, it may be important in a case to know whether the dyspnea is due to a large hemothorax, pneumothorax, pulmonary edema or massive collapse of the lung; whether the circulatory disturbance can be relieved by aspiration or is due to shock or to hemorrhage; whether the temperature is probably caused by infection of the hemothorax or due to some other cause.

The physician's experience in chest examination is helpful, and, what is even more important in times of stress, while the surgeon is constantly occupied in the operating room the physician has more time to study the cases in the ward and to direct treatment in detail.

For these reasons it early became the rule in some of the general hospitals at the bases of the British Army in France to send all cases of chest wounds to specified wards, where they came under the care of a physician who was responsible for them whether operated on or not. This experiment having given satisfactory results, physicians later coöperated with surgeons at some of the casualty clearing stations situated in the forward areas, where most of the early operating was being done, and, in the spring of 1918, the Second British Army appointed a physician for each of their clearing stations to take charge of cases of chest wounds and placed the responsibility for directing this work upon the consulting physician of that army.

The mortality of penetrating chest wounds at the casualty clearing stations was seldom less than 20 per cent. There was a further mortality of about 5 per cent. in cases sent from the clearing stations to the base, and a number of cases, but what proportion I cannot say, died on the field, at the regimental aid posts or at the field ambulances. The total mortality for chest cases, including those complicated by other wounds, was probably not less than 30 per cent.

Therefore, the opportunity to save life by improved methods was clear, many individuals applied themselves to the problem so far as opportunity permitted and great advances in knowledge of the subject were made.

My experience with chest wounds extended over two years and was about equally divided between a general hospital near Boulogne and various casualty clearing stations, to which I was attached from time to time. I have notes, but not as complete as could be wished, of between 400 and 500 cases, probably less than half the number that passed through my hands.

It should be borne in mind that conditions of work vary much in different places, and at different times in the same place, and that methods had to be adapted to conditions as they existed at the time.

None of the hospitals in which I worked had special equipment or facilities for handling chest cases. They were in no way comparable

to the few fortunate hospitals of De Page and others. Nevertheless, the average of efficiency in the British hospitals in France was extremely high. Their staffs of medical officers, nurses and nursing orderlies were ample for ordinary times, but whenever there was heavy fighting on that part of the front, much that might have been desirable to do was perforce neglected and pressure for available beds required evacuation at the earliest possible moment of every case that would not die of the journey. Consequently, no cases could be held for study. At the clearing stations even the severely wounded were seldom retained for more than a week.

Chest Wounds at a Casualty Clearing Station. The first question in chest cases is whether an operation should be performed. In reaching a decision the main points to be considered are the nature of the external wounds and of the missile which caused them, the probable intrathoracic lesions, the condition of the patient and the time elapsed after wounding.

Other problems of interest center around the preoperative and postoperative management, the care of cases not operated on and the diagnosis of the lesions resulting directly or indirectly from the wound. It is these groups of problems rather than those related to operation which are the more likely to interest the physician.

The Preliminary Treatment. He who sees cases of chest wound when they arrive at the clearing station after a trip of eight miles or more in an ambulance, much of the way over rough roads, will be impressed by the exhausted condition of nearly all having severe, penetrating wounds. He cannot but appreciate their need of rest, quiet and warmth. Consequently, he will limit his first examination to absolute essentials. If the patient has much dyspnea it must be known whether air is being sucked into the chest through an open wound and whether there is extensive edema of the lungs, or a large hemothorax or hemopneumothorax requiring aspiration. External bleeding, if present, must be checked at this time.

The sucking wound should be temporarily closed at once, for these wounds produce severe disturbance of circulation and respiration, and closure of them generally affords marked and prompt relief. A stitch is better than strapping, because it holds more surely and permits of subsequent examination of the region of the wound without letting more air into the chest.

Bleeding can generally be controlled by a pad or pack of gauze tightly strapped in place, and the dressing, as a rule, can be removed a few hours later without causing recurrence of the bleeding. A few cases require to be sent at once to the theater on account of persistent hemorrhage, but probably most of these cases die before reaching the clearing station.

Pulmonary edema generally clears up if the patient is put to bed with the chest slightly raised to facilitate breathing, the bed heated and a dose of morphin, $\frac{1}{6}$ gr., and atropin, $\frac{1}{120}$ gr., administered

subcutaneously. Posture seems to me of great importance. The pillow should be arranged like a wedge, with its apex under the lumbar spine and the thick part of the wedge under the shoulders and head. To raise the head only does little good, and, on the other hand, to set the patient nearly upright is to invite further collapse by handicapping the circulation to brain and medulla. If the patient can breathe as well lying flat with only one thin pillow under his head, he should not be propped up at all. Several times I have seen a patient turn gray and the pulse almost disappear after half an hour of sitting up, but improve again after he had been laid down. When nurses have been told to give bed-rests to chest cases they generally place them nearly vertical instead of at the lowest notch. Pillows are preferable because it is not easy to raise a patient very high with them. If the patient is pale and the pulse weak, neither head nor chest should be elevated if morphin will enable the patient to breathe comfortably lying flat. It is difficult to judge of the effect of morphin and atropin on pulmonary edema in cases newly arrived, because the benefit of rest and warmth is undoubtedly great, and morphin was given all cases that were not soon made comfortable without it.

Pain may be slight, but sometimes it is severe enough to embarrass respiration and to be an important factor in causing exhaustion. Most of the cases that I saw at the clearing station had received from $\frac{1}{4}$ to $\frac{1}{2}$ gr. of morphin at the field ambulance, and many were still under its influence when they came to us. Those whose discomfort or pain persisted after getting to bed and who could not be made comfortable by posture were given a second dose of $\frac{1}{6}$ gr. of morphin, which was generally ample. It is a mistake to use more than is necessary, because morphin tends to leave the patient more irritable than before and less able to bear ensuing inevitable discomfort. Chest cases, in my experience, too, are more irritable than any other class of wounded and more difficult to make comfortable. When severe pain persists in spite of reasonable doses of morphin, it suggests a piece of shell lodged in the pleural cavity or friction between the ends of broken ribs. The treatment for either is early operation. In one such case a hernia of lung was found caught between the ends of a broken rib.

Collapsed patients were sent to the resuscitation ward, where they were warmed and the foot of the bed elevated, provided this could be done without inducing dyspnea. Nearly all of these, on account of the nature of their wounds, were urgently in need of operation to prevent or to control infection. Cases that did not soon begin to improve under the treatment above mentioned seldom became decent operative risks. Solutions of glucose and salts were often used by the continuous drip method per rectum, but it is difficult to know what effect it had, because many cases did well without it.

Transfusion of blood will make some cases operable that would otherwise become heavily infected before an adequate operation could be performed. I believe that cases in which large external loss of blood has occurred should be transfused before any severe operation is undertaken. It is not easy to select these cases because the only reliable evidence, as a rule, is the finding of large amounts of blood in the dressings of the patient on arrival; but if dressings were renewed and hemorrhage stopped at the field ambulance, evidence of hemorrhage is lacking. On the other hand, collapse from shock or from exhaustion simulates conditions resulting from hemorrhage. When the presence of a large hemothorax suggests that loss of blood has been chiefly internal, transfusion seems to me contra-indicated for two reasons: (1) lest it add to existing circulatory embarrassment directly, and (2) lest it induce further internal hemorrhage. In abdominothoracic wounds with intraperitoneal hemorrhage transfusion is not likely to do good until after operation. It is dangerous, I think, whenever dyspnea is marked, whether associated with large hemothorax, pneumothorax, pulmonary edema or massive collapse of the lung.

Diagnosis. The difficulty of diagnosis in some serious cases will be apparent when it is realized that the patient needs rest, that examination fatigues him, that he must be roentgen-rayed before operation, and that he should be in the theater and in condition to stand the operation with the least possible delay.

Moreover, he cannot take a deep breath; his apex impulse is seldom palpable at this time; the anterior portions of the lungs are often hyperresonant; frequently there is subcutaneous emphysema of parts of the chest wall, causing a tympanitic percussion note; in other parts there are wounds; both lungs may be damaged; there may be pulmonary edema, bilateral hemothorax, massive collapse on the unwounded side, and on the wounded side simple hemothorax, pneumothorax, more or less collapse, hemorrhagic infiltration, more or less extensive, or any combination of these.

Displacement of the heart in the *same* direction may be caused by massive collapse on one side, hemothorax on the other, or by both together.

Moreover, wounds which do not penetrate the pleura frequently cause hemoptysis, not rarely hemothorax, and sometimes extensive collapse of the lung.

On the second day after wounding, and subsequently, patients can be examined more easily than on the first day. They breathe more naturally, and the signs, for some reason which I do not understand, seem to be more definite.

Fluoroscopic examinations were made in all cases having retained missiles, and in many others, as an aid to diagnosis of the intrathoracic condition. Sometimes a foreign body which had entered the chest would be found in the abdomen or liver, or the wound of

entrance and the position of the foreign body in the chest might show that it must have injured the diaphragm. The roentgen-ray examinations were made in the standard position with the screen, the patient lying flat on his back on the stretcher with a half-blown air cushion under the head and shoulders. Displacement of the heart was looked for and the shadows were described. The radiologist could distinguish hemothorax, as a rule, without difficulty. With hemothorax of large or moderate size the heart was seen to be displaced toward the opposite side. The diaphragm was visible, as a rule, when the hemothorax was small and sometimes when it was of moderate size. The position of the diaphragm in these cases when seen was regularly reported by Capt. Finzi, R.A.M.C., as being elevated and its movement restricted on the side of the hemothorax. Another radiologist frequently reported the diaphragm depressed and flattened with hemothorax, but I think that the raised position was the more usual. Hemorrhage into the lung along the track of the missile often gave a shadow distinctly visible. Shadows in the opposite lung not due to direct injury were sometimes attributed to more or less extensive collapse of the lung. The condition was spoken of as "contralateral collapse." The shadows were wedge-shaped, the base toward the lateral chest wall and the apex toward the spine. Generally, there was an area of better illumination at the extreme base and in the costodiaphragmatic angle which served to differentiate the condition from hemothorax.

Preliminary Aspiration. In a small proportion of cases in which a large hemothorax, or hemopneumothorax exists it may cause a positive intrathoracic pressure on the affected side with the result that dyspnea renders the patient's condition unsatisfactory for operation. Moreover, opening the chest would lead to a sudden reduction of this pressure, and in cases in which the mediastinal contents are freely movable, might result in added disturbances of circulation or respiration. Therefore, in such cases, it has seemed to me best to aspirate as a preliminary to operation, and to endeavor to leave the intrathoracic pressure at approximately that of the atmosphere, or, in other words, to withdraw only as much as can be easily obtained without suction. To empty the chest so soon after wounding would be to run the risk of recurrent hemorrhage.

By a series of observations of intrathoracic pressure in hemothorax[2] measured in centimeters of water, it was found that intrathoracic pressure might sometimes be reduced by as much as 12 cm. by the removal of not more than 780 c.c. of fluid. The negative pressure so produced would be suddenly neutralized the moment the chest was opened at operation. This last disadvantage, however, can be overcome in large measure by the use of gas-oxygen anesthesia and a positive pressure of the anesthetic while the chest is

[2] Shattuck and Welles: Quarterly Jour. Med., April, 1919.

open. Major Geoffrey Marshall, R.A.M.C., when in charge of anesthetics for the Second British Army in 1918, used positive anesthetic pressure for thoracotomy operations with marked success.

POST-OPERATIVE MANAGEMENT. *Post-operative Aspiration.* When, by a radical operation, the hemothorax has been evacuated, bone fragments and foreign body removed and the chest closed, fluid soon begins to collect in the pleural cavity. Its rate of increase is probably determined chiefly by the amount of residual infection. To limit this accumulation and to promote reëxpansion of the lung it became the practice to aspirate once at least after operation. The rule which I followed was to aspirate after twenty-four hours had elapsed and again two days later. In the most favorable cases 200 or 300 c.c. of fluid and some air were obtained at the first tap, and so little fluid at the second that further tapping was superfluous. In all instances a specimen of fluid was sent to the laboratory for aërobic and anaërobic cultivation, so that infection, when present, should be quickly recognized.

Lockwood and Nixon[3] reported excellent results in a number of infected chests which had been cleaned out as far as possible by operation, closed and aspirated. In spite of infection demonstrated after operation they aspirated repeatedly instead of resorting to secondary drainage. I have no doubt that their example could be followed to advantage in certain types of cases, but believe that if aspiration is to be relied on to keep an infected chest clear of fluid it is essential to have the use of a portable roentgen-ray apparatus which can be used in the ward. By this means, and by no other, I think, can there be any assurance that all the fluid has been in fact removed. Lockwood and Nixon used such an apparatus and considered it indispensable.

For two days after severe operations morphin was used freely to relieve pain and to check the restlessness of discomfort. Cases doing well did not require its longer continuance.

Pulmonary Edema. Some patients who had been operated on and others who had not were troubled by attacks of dyspnea and wheezing or rattling in the chest associated with light frothy expectoration. The attacks came on sometimes late at night, in other cases in the evening and in still other instances the symptoms began in the daytime.

The mildest attacks were those that came on late at night. The condition in these cases was quickly relieved by a dose of morphin $\frac{1}{6}$ gr., and atropin, $\frac{1}{120}$ to $\frac{1}{100}$ gr., subcutaneously. When the attack began in the evening relief was temporary, and a second dose was required in the course of the night. When frothy expectoration first appeared in the daytime it yielded less readily to drugs, and the edema usually became more marked during the night.

[3] British Med. Jour., January 26, 1918, p. 105.

The frothy expectoration occurred in two groups of cases, namely —in the later stages of cases that were more or less infected and in the early stages of severely wounded cases, especially when exhausted by travel. In the later stages the froth was white, but sometimes it was mixed with the purulent sputum of bronchitis. The response to drugs was best when there was no bronchitic sputum and correspondingly less when it predominated. Pulmonary edema coming on in the daytime was a bad prognostic sign.

Among the group of cases in which pulmonary edema appeared early there were some which arrived at the clearing station in this condition. As might be expected so soon after wounding the froth was tinged with blood and was often mixed with thick mucus or blood. In these cases also the result of medication seemed to depend a great deal on whether or not the sputum consisted chiefly of froth or mainly of viscid material and blood.

Cases not Requiring Early Operation. These cases consist of two groups, namely—those whose condition is apparently hopeless and those which may be expected to do well without operation.

Some of these last require aspiration for relief of symptoms or to hasten convalescence, and others develop intrathoracic infection, calling for operative interference later. Their special problems are discussed in the paragraphs which follow.

Intrathoracic infection in chest wounds commonly follows penetration of the chest by a large shell fragment. It seldom results from a bullet or shrapnel ball except in the comparatively small number of these cases having extensive bone damage. Early operation is indicated in the cases likely otherwise to become infected. The remainder should not be operated on unless evidence of infection appears later. The important thing is to watch for signs of developing infection and to recognize it promptly if it appears. Nearly all cases of penetrating wounds have enough hemothorax to make it possible to withdraw a sample to be cultured in the laboratory. This should be done for all cases of hemothorax that are to remain in the hospital long enough to get a report.

Fever of a moderate degree is the rule in sterile hemothorax, but after a few days it begins to subside. Case I is an example, but in this case the fever lasted considerably longer than is common in the absence of infection. The two negative reports on the chest fluid and the final subsidence of the fever indicate that if infection was present at all it was inconsiderable. Infection generally begins to give signs on or after the third day, although cultures of chest fluid will often show its existence earlier.

Infection should be suspected when the temperature and pulse do not show a downward tendency after a few days, when the amount of fluid in the chest seems to be increasing, when the patient's condition does not rapidly improve, or when after temporary improvement he becomes abnormally irritable, complains of intrathoracic pain and the temperature begins to rise again.

An early sign of infection to which Capt. Adrian Stokes, of the Royal Army Medical Corps, called my attention is well-marked hemolysis in chest fluids obtained within three days of the wounding. Hemolysis developing later is so common in chest fluids which remain sterile that it has no considerable diagnostic value after the first three days.

Infection with streptococcus causes a rapid increase of fluid in the chest. The infection may develop early or late, and when it comes early may be combined with infection by other organisms. The streptococci found in the chest were of two principal types, hemolytic and non-hemolytic. Both organisms generally caused serious infection, but the hemolytic type seemed to be particularly virulent. The mortality of infected hemothorax following *early* resection of a rib and open drainage is very high, so much so that anything which offers hope of reducing it should be tried. The mortality is lower when the infection does not appear until the end of the first week or later. Open drainage after the first week disturbs the respiration and circulation far less than is the case when it is performed earlier. This can be explained on the supposition that adhesions have formed and the cavity become walled off by a thick layer of fibrin. Certain it is that in these cases of late operation very little air passes back and forth through the drainage tube, whereas in cases of early drainage the reverse is true and the patient can only be made comfortable by preventing the inrush of air during inspiration by applying some kind of valve as a part of the dressing.

Aspiration of Infected Chests. In the summer of 1918 I treated eight or nine cases of early infected hemothorax by daily aspiration for a week before resection was performed. It was hoped in this way to limit the infection to a smaller cavity and to reduce mortality. After each aspiration the patients generally felt more comfortable, and in several cases the pulse and the temperature dropped in the course of a few days to nearly normal, only to rise again later. The attempt to reduce the size of the cavity to be drained was not apparently successful. In some cases the reduction of toxemia was slight and transient, in others marked benefit resulted, but was followed after a few days by recurrence of toxemia. In all cases emaciation developed rapidly. The failure to get all the results hoped for can be attributed to the difficulty of draining completely by aspiration a collection of fluid containing large and increasing amounts of coagulum and having a marked tendency to collect in pockets.

No case of hemolytic streptococcus infection was included in this series. One case had gas-bacillus infection. His condition on admission was such that operation was not then considered. Following aspiration of the chest, little if any walling off took place. Two small transfusions gave temporary benefit and resection was finally performed, but the patient died after about two weeks.

The other cases had non-hemolytic streptococcus. It seemed to me that the marked temporary improvement shown by some of them indicates that aspiration within the first five days followed by open drainage is probably less dangerous than open drainage performed earlier. Operative drainage, I think, should not be delayed as much as a week, but should be performed the moment improvement after aspiration ceases. Control observations by means of a portable roentgen-ray apparatus would have been valuable.

Pneumococcus infections of the pleural cavity tend to die off quickly and some of them can be cured by aspiration alone. The same is true of some cases of staphylococcus infection. Cases of gas-bacillus infection may show very marked symptomatic improvement after aspiration. Unless there is concomitant infection with other organisms it is probably good practice to aspirate them once at least before operation. This should certainly be done if accumulation of gas or a large amount of fluid embarrasses respiration or circulation. The gas bacillus is by no means as virulent in the pleural cavity as it is in the muscles.

Aspiration cannot be relied on for more than temporary relief for cases having large retained fragments of shell plus the cloth and bone fragments usually carried in by them. Early radical operation offers the only hope for these cases. Aspiration as a *cure for infection* should be tried only when the infection develops late, is of a mild type or follows a radical cleansing operation.

A portable roentgen-ray apparatus would add materially to the safety and advantage of this method, because plates could then be taken without fatiguing the patient and it would be possible to determine after aspiration whether all the fluid had been removed.

Hemothorax. For purposes of description, hemothoraces can be divided into three classes: the small, in which the pleural cavity contains not more than 500 c.c. of bloody fluid; the moderate, containing from 500 to 1000 c.c.; and the large, hemothoraces of from 1000 c.c. upward.

The physical signs of a small hemothorax are dulness below the angle of the scapula, with all other signs diminished and more or less aëgophony. The aëgophony is not pronounced, but, I think, it is the most valuable single sign of fluid in these cases.

So far as I have been able to ascertain from the somewhat conflicting reports of various radiologists the diaphragm is usually high and moves little from the first days after wounding. It was early learned that exploratory tapping to demonstrate the pressure of small hemothoraces was generally successful even when signs were very slight, provided the puncture was made midway between the spine and the posterior axillary line in the interspace lying under the angle of the scapula. To uncover this interspace the hand of the patient was carried to the shoulder of the opposite side. Exploratory taps made lower down frequently failed to show the presence

of fluid. In other words, the fluid in a small hemothorax lies higher than is the case with pleural effusion or the common form of empyema secondary to pneumonia. In the early days of hemothorax it seems improbable that settling out of fibrin or the formation of adhesions in a *sterile* hemothorax could account for failure to obtain fluid lower down.

These observations strengthen the view that the diaphragm in small hemothoraces is generally at a high level.

The apex impulse of the heart is not notably displaced, but the roentgen ray may show slight displacement away from the fluid, indicating a reduction of negative pressure in the affected side of the chest. Case III is a typical example of small sterile hemothorax.

The hemothorax of moderate size gives physical signs like the small one, but more marked. Cardiac displacement cannot often be demonstrated in the first few days after wounding without putting the patient through a more rigorous examination than seemed ordinarily justifiable or necessary. The apex impulse is often impalpable at this stage. Symptoms in these cases do not render aspiration urgent.

When I began to examine cases of hemothorax I assumed that the changes in the breath sounds over the retracted lung near the upper limit of the fluid would be the same as in the ordinary case of pleural effusion. I expected the breath sounds to be diminished in intensity but typically bronchial in character. It was found, in most cases, however, that their quality was not typically bronchial, but rather more amphoric. They might perhaps have been described as bronchoamphoric, partaking, as they did, of both qualities (Case III). Sometimes they were almost purely amphoric as in typical pneumothorax. Nevertheless, exploratory tapping over the point of greatest intensity of this breathing yielded over and over again fluid only. Neither was air often obtained, as below stated, by aspiration. (See Pneumothorax.)

The intensity of the breath sounds over a hemothorax is almost invariably diminished above and still more diminished or absent below.

Retraction or flattening of the chest-wall below the clavicle in front or below the angle of the scapula behind or at both points was observed in a great many cases of hemothorax examined at the 22d General Hospital. This phenomenon seemed to be less frequent and less marked the first few days after wounding than after a week or more from the date of injury.

This condition associated, as it appeared to be, with a high diaphragm, points in these cases to collapse of the lung over and above that induced by the mere presence of fluid. (See Massive Collapse below.)

That the diaphragm may be depressed, and probably is depressed, as a rule, by large collections of fluid or of fluid and air in the pleural

immobile and retracted; there will be extensive dulness; the breath sounds may be bronchial or absent; and the roentgen rays will show a shadow over the right side of the chest, a high, immobile diaphragm, and the dorsal portions of the ribs will form a more acute angle with the spine on the right than on the left.

Cases of such extensive collapse are easy to recognize, but they are rare. Lesser degrees of collapse are probably common but difficult to diagnose with certainty. The possible presence of more or less collapse in either lung in any case of chest wound renders interpretation of physical signs difficult and uncertain. A common error is to mistake the collapse for pneumonia or for fluid. The position of the apex impulse is the key.

Chest Wounds at the Base. The problems at the base differ from those at the clearing station mainly from the fact that patients arrive later, that most of the bad cases have been eliminated by death or improved by operation, and that, as a rule, the patients arrive too late for radical operation, designed to prevent infection.

What is most needed is to combat existing infections of the parietes or intrathoracic structures, and to keep a sharp lookout for complications, and for infections which may develop late.

Pulmonary edema is sometimes induced by the journey and develops at night in some infected cases. The treatment has been described above.

Massive collapse is seen at the base as well as in the zone of the armies.

The questions relating to sterile hemothorax can be most advantageously studied at the base.

Summary. Under the war conditions met with a physician could render valuable service either at an advanced operating center or at a hospital in the rear by coöperating with the surgeon who did the chest operations, or even by becoming responsible for the treatment of all cases of chest-wound, whether operated on or not. The selection of cases for operation, their preliminary treatment and after-care were left mainly in the hands of the physician after he had learned to select the types of cases which operation could be expected to help.

When urgency of work does not require the constant presence of the surgeon in the operating room, however, he will do well to take personal charge of the post-operative cases himself, and should confer with the physician whenever doubt arises as to the best course of treatment to pursue either before or after operation.

There are many points of technic still to be worked out regarding the best methods of operating and the care of post-operative chest cases, which the surgeon can never appreciate unless he himself follows closely the cases he has operated on.

Close coöperation between one physician and one surgeon is essential to the best results and a strong nursing staff is absolutely necessary if treatment is to be satisfactorily carried out.

The management of cases not requiring operation, the diagnosis of intrathoracic lesions and the treatment of some of the most serious symptoms is essentially medical work.

Aspiration may be useful (*a*) as a preliminary to operation or to relieve symptoms when a large hemothorax or hemopneumothorax exists; (*b*) it should be performed after thoracotomy and closure of the chest; (*c*) infected hemothoraces should, in some cases, be aspirated for several days before open drainage is resorted to. A few will recover by aspiration alone.

Sterile hemothoraces, probably, should not be aspirated, unless causing symptoms, until a week or more after wounding, lest infection be drawn into the pleural cavity.

Replacement with oxygen is useful in cases of certain types.

It is a pleasure to thank Surgeon-General Sir John Rose Bradford and Colonel A. B. Soltau, of the British Medical Service, for helpful advice and information.

CASE I.—J., admitted to the casualty clearing station October 4, 1917, in the morning. Wounded probably on the day before. On arrival the patient was collapsed. He had multiple small wounds of the left shoulder and a slightly larger wound in the lower left axilla. The wounds looked as if produced by a shell or grenade, but the fragment which struck the lower axilla was probably the only one to penetrate the chest. None of the wounds were severe. The signs indicated a very large hemothorax. The patient was kept under morphin for the first twenty-four hours. After that he was comfortable and had little dyspnea.

A roentgen-ray examination of a few days later showed the heart displaced considerably to the right and a dense shadow over the left chest. The left diaphragm could not be located and showed no sign of movement. An irregular shell fragment, about 1.5 cm. in greatest diameter, was seen near the root of the left lung.

October 12. Aspiration was postponed in this case until the ninth day because symptoms did not require it. About 1000 c.c. of dark colored bloody fluid was withdrawn. It ran in a steady stream without requiring suction. No cough or distress resulted. Immediately after the aspiration, dulness was diminished on the left and the cardiac displacement seemed to have diminished.

October 13. The signs on this day indicated no less fluid in the chest than before aspiration was performed. By a second aspiration about 1000 c.c. of fluid like the first was again withdrawn. It flowed in an even stream as before and its withdrawal was accompanied by none of the discomfort usually incident to expansion of the lung when this quantity of fluid is removed.

October 14. The patient looked decidedly paler than he had looked before the first aspiration and the chest signs still indicated the presence of a large amount of fluid.

It was believed that the chest had filled up again and that hemorrhage had probably played a considerable part in replacing the

fluid. Against this is the fact that the pulse-rate as shown on the appended chart did not change. In favor of hemorrhage is the lack of signs of expansion of the lung while the aspiration was in progress, the absence of respiratory movement of the injured lung shown by the steady flow of the fluid, the increased pallor of the patient, the unchanged color of the fluid at the second aspiration showing that

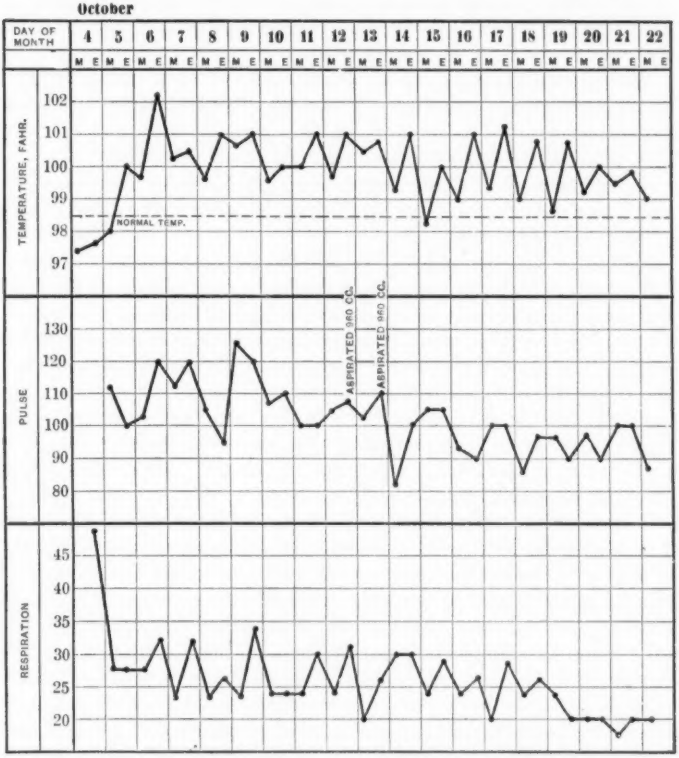

FIG. 1.—Case I. Large hemothorax aspirated on the ninth and tenth days after wounding. Hemorrhage into the pleural cavity apparently recurred on both occasions.

it still contained a like proportion of blood, and the absence of evidence of infection, as shown by the gradual fall of temperature and pulse to near normal and two negative reports on specimens of chest-fluid cultured in the laboratory. Reaccumulation of fluid to a marked degree after aspiration of a hemothorax generally indicates infection, but the fluid poured out in these cases is serous and dilutes the remaining blood, so that the resulting mixture is lighter in color.

CASE II.—M., admitted to 22d General Hospital, April 27, 1917.

History. Wounded on April 23, four days ago, probably by machine-gun bullets, one of which passed through the left arm near the elbow and another through the lower *left* chest near the axillary side. He spit up no blood after being wounded or at any other time. Shortness of breath came on soon after wounding, preventing him from walking.

Physical Examination. Wounds small and clean. Bone damage slight.

Heart. Dulness mainly to *right* of sternum. Impulse distinctly felt above the *right* nipple.

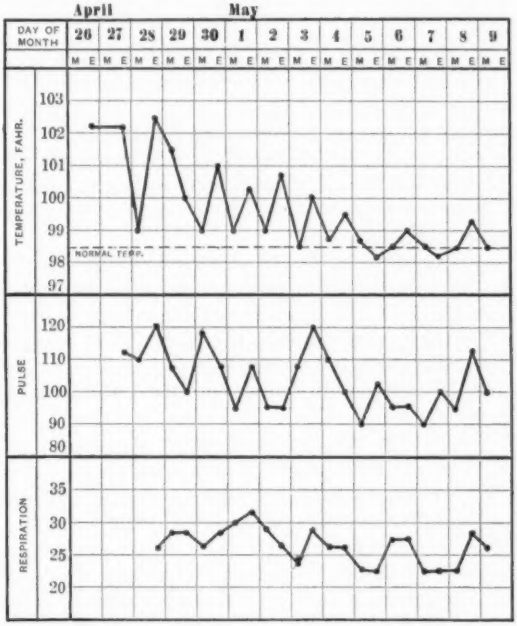

FIG. 2.—Case II. Massive contralateral collapse.

Chest. Below *right* clavicle percussion note tympanitic and breath sounds amphoric rather than bronchial. Below this on the right and in the right axilla there is slight dulness, breath sounds diminished and rather amphoric in quality.

The *right* back showed slight dulness from mid-scapula to base. Tactile fremitus was absent over this dull area. The breath sounds were amphoric in quality, loud above and faint below.

The *left* chest showed no dulness, and no modification of breath sounds was observed.

April 30. The heart impulse is now felt one inch within the *left* nipple. Heart dulness still increased to right.

Below the angle of the *right* scapula definite dulness persists. At the right base the dulness has a tympanitic quality.

May 1. Roentgen-ray report: "Left chest apparently normal. Lower half of right chest somewhat cloudy. Diaphragmatic line obliterated. Dense shadow up to sixth intercostal space. Apex of lung appears normal. Heart normal in size, slightly displaced to *left*." (?) (Probably this is an error or should read right.)

May 2. Motion of chest wall about equal on both sides; no retraction of chest wall. Dulness persists as on April 30.

Heart nearly in the normal position.

Impulse felt one inch within the *left* nipple.

May 4. Exploratory tap below angle of right scapula; nothing obtained.

May 9. Evacuated to England in good condition.

NOTE.—The observations above recorded were made before collapse had been recognized by the writer. They are, therefore, not as complete as they should be. The signs described are typical of collapse and can best be explained by that diagnosis. The fever was probably caused in part if not wholly by slight infection of the wounds. A loose fragment of bone was removed from the dressing on the back on April 30.

CASE III.—R., admitted to 22d General Hospital July 7, 1916.

History. Wounded July 1, probably by a bullet which entered in the upper left axilla and passed out below the angle of the left scapula. Walked six or seven miles, he thinks, after being wounded. Has had severe cough from the beginning and raised a good deal of blood at first. Now raises little, but sputum is occasionally bloody. Has much dry cough.

Physical Examination. Tongue heavily coated.

Heart. Negative and apparently not displaced.

Lungs. Entire front of *left* chest is hyperresonant. Breath sounds increased in front on both sides, more on right than on left. Quality of breath sounds normal. Slight dulness at base of left axilla and in left back below angle of scapula. Over the dull area in the back tactile fremitus is absent. In this area the voice sounds are diminished and show aëgophony. In a small area between the wound and the spine the breath sounds are more amphoric than bronchial. Below this they are faint.

Castor oil was prescribed.

July 8. A small hemorrhage from wound in back during the night.

July 11. Wound in axilla healed. The one in back nearly so. Few rales heard at left back. Below angle of scapula on left slight dulness persists. Tactile fremitus diminished. Breath sounds amphoric. General condition much better.

July 15. A few rales at the left base behind. Breath sounds louder and more vesicular. Voice sounds still slightly aëgophonic. Front of the chest negative. Slight pain over lower ribs in front.

July 18. Dulness persists but breath sounds are louder and extend to base. They are bronchovesicular in quality.

There is still pain on cough over left lower ribs in front. The wounds are healed and the patient looks very well.

Marked for evacuation to England as a walking patient.

NOTE.—This is a typical case of small sterile hemothorax. The fever may perhaps be due to slight infection of the wounds or perhaps to the hemothorax itself. Initial fever is the rule in such cases even when there is no demonstrable infection of the hemothorax.

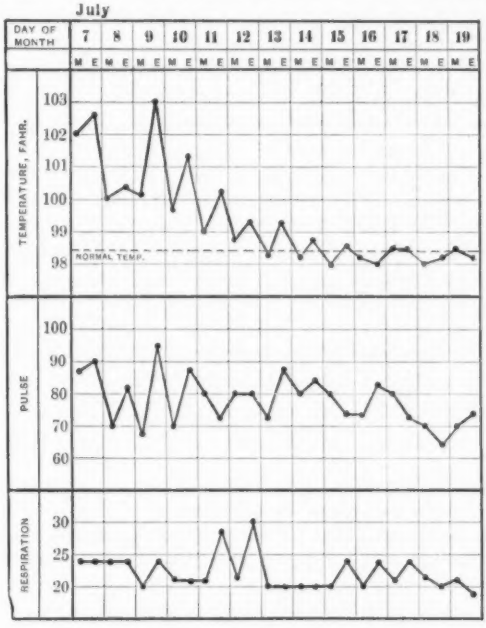

FIG. 3.—Case III. Small sterile hemothorax.

CASE IV.—Notes received with the patient from the casualty clearing station: W., "shrapnel wound of neck. Wounded June 17, 1917. Roentgen rays show foreign body lying in posterior mediastinum. Hemothorax, fluid sterile.

June 30. Aspiration attempted but very little fluid obtained. General condition much improved. Temperature 101° to 102° until June 20, gradually falling after that to normal. Normal after June 27."

July 3. Admitted to 22d General Hospital.

Physical Examination July 3. Apex impulse not visible or palpable. Cardiac dulness considerably increased to right of sternum. Sounds best heard in median line and not heard in nipple line.

Dulness in left chest from third rib in front, from top of axilla

and from spine of scapula to base. The lower part of the chest is flat to percussion. Tactile fremitus diminished above and absent below. Breath sounds are distant, bronchial above and absent below. Aëgophony is marked above and diminished below. Right chest negative.

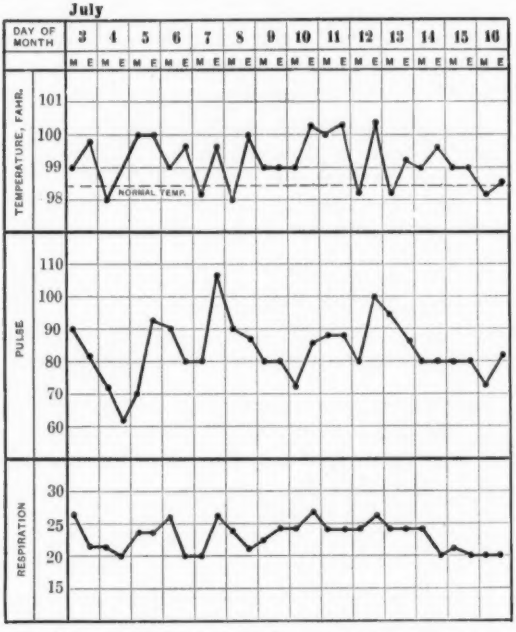

FIG. 4.—Case IV. Aspiration of a hemothorax and replacement by a nearly equal amount of oxygen showing maintenance of intrathoracic pressure almost unchanged.

July 4. Aspirated from left back 1700 c.c. of bloody fluid. Simultaneously 1600 c.c. of oxygen at atmospheric pressure was put in.

The intrathoracic pressure measurements made with a water manometer were as follows:

Before aspirating { Expiration + 3cm. / Inspiration atmospheric

After aspirating { Expiratory + 2 cm. / Inspiratory 0 (or at)

Reduction of inspiratory pressure = 0.

The following measurements from the case of C. serve for comparison. Aspirated 800 c.c. bloody fluid plus an unknown amount of air.

Before aspirating { Expiration +3 cm. / Inspiration −2 cm.

After aspirating { Expiration −2 cm. / Inspiration −14 cm.

Reduction of inspiratory pressure = 12 cm. of water.

THE HEART IN BRONCHOPNEUMONIA: OBSERVATIONS ON THE ACTIVITY OF THE HEART AND ITS RESPONSE TO DIGITALIS MADE DURING THE RECENT EPIDEMIC.

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During the recent epidemic of the so-called influenza in New York as elsewhere the hospital facilities were taxed to the limit. To assume its share in this emergency the Presbyterian Hospital assigned for this purpose 130 beds. These were thus occupied during the months of October and November, with the number gradually diminishing toward the spring. These in combination with a large number seen in consultation with physicians in private practice have given us an opportunity to formulate our impressions on a considerable group of cases.

The present presentation is concerned only with the condition of the adult heart in this epidemic and the manner in which it is affected by digitalis in those who developed bronchopneumonia.

The outstanding features of the typical cases of pneumonia as we have seen them are:

1. The bluish-red pharynx without exudate.
2. The substernal distress associated with the cough.
3. Expectoration copious, mucopurulent and blood-streaked.
4. The absence of evidence of pleurisy.
5. The leukopenia.
6. A bluish-red cyanosis of the skin and mucous membranes out of proportion to the extent of the pulmonary involvement as evidenced by the physical signs or the radiographic plates.
7. The insidious development of the physical signs of consolidation in patches and a change to a bronchial quality of voice and breathing which may appear only after some days or may never become evident during the whole course of the disease.
8. The respiration always accelerated but rarely above 40, except in the cases with a fatal outcome.
9. Fever, usually continuous at a level somewhere between 103° and 105°, sometimes quite irregular, with marked remission, lasting from five to fourteen days, occasionally longer and terminating in those who recover by a drop to the normal, which occupies a period of from twelve to forty-eight hours.
10. Heart-rate always somewhat accelerated, 90 to 110, but as compared with the temperature nearly always relatively slow. In the fatal cases the pulse-rate sometimes gradually becomes more rapid, but, as a rule, there is only marked acceleration in the terminal hours.

11. Heart action regular, sounds of good quality and unchanged except when the consolidation is very extensive, when the pulmonic second sound may be accentuated. Murmurs do not develop. No evidence of engorgement of the right heart.

How is the Heart Affected in These Cases? It appears to me that in the majority of these patients the heart does its work remarkably well. The cardiac activity seems to be very similar to the conditions which we observe in uncomplicated typhoid fever. We have (Fig. 1) a relatively slow pulse-rate, a low blood-pressure, both systolic and diastolic, with a fairly good pulse-pressure, a normal rhythm which rarely becomes irregular. I have observed extrasystoles on a few occasions, but not once have I found the development of complete irregularity. The heart sounds are of good quality and murmurs rarely develop. Undoubtedly the marked cyanosis has suggested the thought that the right heart

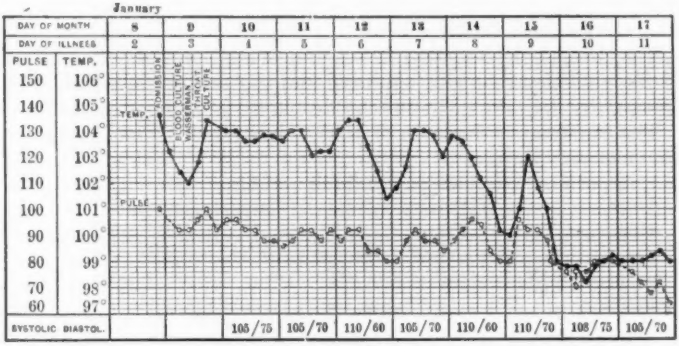

Fig. 1.—Severe uncomplicated bronchopneumonia; recovery. Relatively slow heart-rate; no digitalis administered.

was failing, but if one observes his patients closely he will rarely find other signs to corroborate this point of view. There is no increase in cardiac dulness to the right, no marked epigastric pulsation, no stasis, no exceptional pulsation or distention of the veins discharging into the right auricle. The cyanosis which is so prominent a feature must be explained on grounds other than insufficiency of the right heart. I am personally convinced that the ordinary cause of death is not heart failure. The heart usually preserves its efficiency up to a few hours before the termination, and then only gives way against overwhelming odds (Fig. 2).

The postmortem material which we have been able to study has been regrettably meager, but the few uncomplicated cases in which the heart was carefully studied by Dr. A. A. Eggstein showed only a moderate degree of myocardial degeneration and failed to lend weight to the view that death was due primarily to myo-

cardial insufficiency. A number of our cases died with evidence of pulmonary edema, but even in these the heart seemed to be performing its part with reasonable efficiency.

The fatal termination presented the picture of an overwhelming toxemia. As evidence of this may be cited the extreme cyanosis, the leukopenia, the diminished coagulability of the blood, the fever, the delirium which so frequently develops in the severe cases and in the less severe that are protracted, and the great mortality in pregnant women. The mechanism of the action of the toxins and the tissues most vitally concerned have occupied our thought, and some of our studies have been directed to the solution of this problem, but thus far with inconclusive results. Certain of the phenomena point to a defect in the capillary wall as an important element; others suggest fundamental alterations in the elements of the blood. Incidentally, it may be stated that

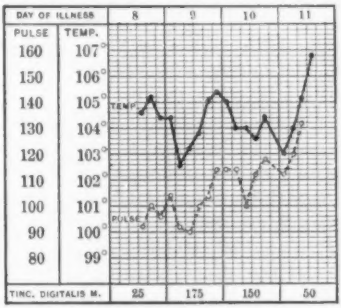

FIG. 2.—Fatal case of uncomplicated bronchopneumonia, showing a relatively slow heart-rate, becoming rapid toward the termination in spite of efficient digitalization.

a number of observations on the carbon dioxide content of the blood showed this to be normal in every instance. This would indicate that the cyanosis is not due to a condition of acidosis.

This view, that the fatal termination in these cases is due to causes other than cardiac failure, is reinforced by the reports of a number of competent pathologists and clinicians. Symmers[1] says: "Both the naked-eye and microscopic appearances of the heart muscle fibers, however, are in the majority of instances indicative of a surprisingly excellent state of preservation. Cloudy swelling, in my experience, is exceptional." Lyon[2] reports from the Walter Reed Hospital: "In the entire series the heart showed no evident pathological changes." Lamb and Brannin[3] in reviewing the epidemic at Camp Cody comment as follows: "Gross changes in the heart or pericardium were not encountered. We found no

[1] Jour. Am. Med. Assn., 1918, lxxi, 1485.
[2] Ibid., lxxii, 927.
[3] Ibid., p. 1060.

evidences of dilatation on either side; the muscle was firm; the ventricles, usually contracted, contained a small amount of dark, semiclotted blood. The "chicken-fat" clots, often observed in pneumonia and slow death, were not found." Brem, Bolling and Casper[4] in their report from Camp Freeman say: "The pulse-rate was slow in proportion to the fever and the blood-pressure was low, the systolic pressure frequently being 100 and the diastolic pressure from 40 to 50. The pulse-pressure was good and there were no signs of cardiac insufficiency except in the fatal cases after the onset of respiratory insufficiency and shortly before the end. The danger never appeared to arise from the effect of the infection on the cardiovascular mechanism."

The observations of Synott and Clark[5] gleaned from experiences at Camp Dix were as follows: "The outstanding feature of the disease was the extreme toxemia noted in the serious cases. . . . Very often the cyanosis came on suddenly in patients who had been doing well. It was not due to cardiac dilatation. The pulse was often slow, full and regular in such cases, and remained so, with a rate under 100 almost until death. The disparity between temperatures and pulse was striking."

DIGITALIS. We made an attempt to determine the action and value of digitalis in these hearts. For this purpose two preparations only were used. A tincture made by the hospital pharmacist, and which has proved potent and efficient clinically both in the course of these patients and upon other patients not of this series which were being treated at the same time in this institution, and "digifolin" (Ciba) in ampules, a solution of digitoxin and digitalin, which proved to be an active preparation, well adapted for intravenous use; the latter preparation was not only found active by clinical observation, but was also standardized by the frog method for us by Dr. Lieb, in the laboratory of experimental pharmacology of the College of Physicians and Surgeons. The tincture was used only by mouth and digifolin only intravenously. In a considerable number of cases the efficiency of our digitalis and evidence of a dosage sufficiently large to modify the activity of the heart under observation was secured by electrocardiographic records. These showed a prolongation of the P–R interval, changes in the contour of the T-wave[6] and occasionally a partial auriculoventricular block, conclusive proof that we were effectively digitalizing the myocardium (Figs. 5, 6, 7, 8, 9, 10 and 11).

The routine method adopted in the hospital was to begin the administration of digitalis as soon as the diagnosis of pneumonia was reasonably sure. There was given of the tincture 25 minims every four hours for six doses, which was then reduced to 15 minims

[4] Jour. Am. Med. Assn., 1918, lxxi, 2139. [5] Ibid., p. 1817.
[6] Cohn, Fraser and Jamieson: Jour. Exp. Med., 1915, xxi, 593.

every eight hours, and continued, with modification according to the individual indications, throughout the course of the disease. Patients who developed symptoms of toxemia very rapidly or who were found in this condition on admission were frequently given 15 to 30 minims of digifolin intravenously, and this was repeated every four hours up to three or four doses, after which time the tincture was usually substituted. We feel that our dosage was sufficient to digitalize the heart in all cases, and this was conclusively proved in those from whom electrocardiographic records were secured.

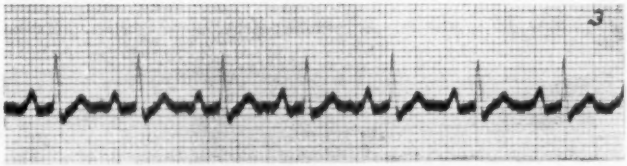

FIG. 3.—Sixth day of disease, after tincture of digitalis 150 minims. Rate 107. P–R = 0.19 second.

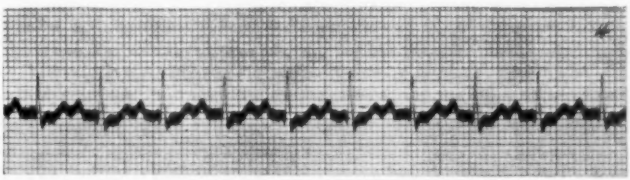

FIG. 4.—Eighth day of disease, after tincture of digitalis 225 minims. Rate 136. P–R = 0.20 second. Note change in T wave.

FIGS. 3 and 4.—Case of bronchopneumonia terminating fatally on the tenth day of the disease. Admitted on the fourth day with a heart-rate of 104. The rate continued to increase in spite of efficient digitalization and reached 160 twenty-four hours before death.

For the sake of comparison and control a considerable number of cases were from time to time selected at random and treated by methods identical in all respects, except that to these no digitalis was administered.

The results of our observations may be summarized by saying that absolutely no difference in the course of the disease could be observed in the two series. The hearts of those patients treated without digitalis and those to whom it was given behaved in a similar manner, except that the electrocardiograms of those receiving digitalis showed the characteristic changes, and in two instances an arrhythmia developed which proved to be due to a condition of partial heart block (Figs. 6, 7, 8, 10, 11 and 12). The patients to whom digitalis was given ran their course without a change in the pulse-rate which could in any way be attributed to the

drug. Some held a rate below 100 throughout their course, others which had a more rapid rate failed to respond by diminished rate to increasing doses of the drug (Figs. 2, 3 and 4). The terminal

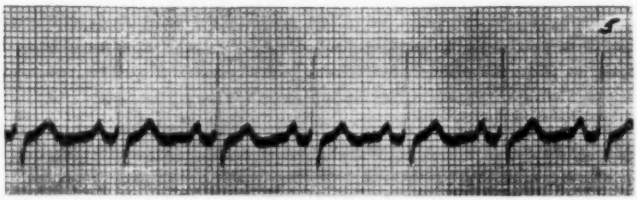

FIG. 5.—February 6, after tincture of digitalis 130 minims. P–R = 0.16 second.

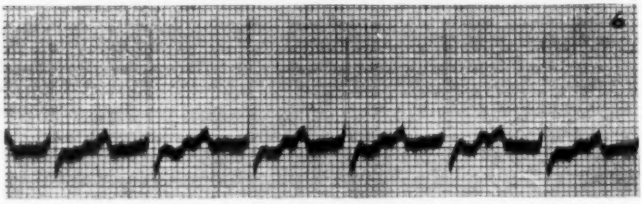

FIG. 6.—February 10, after tincture of digitalis 480 minims. P–R = 0.36 second. Note change in form of T wave. No digitalis after this.

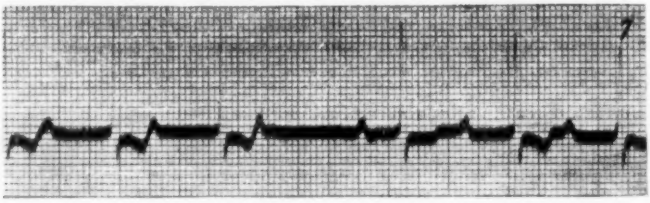

FIG. 7.—February 13. Partial A–V block. P–R (variable) = 0.48 ± second. Note change in T wave.

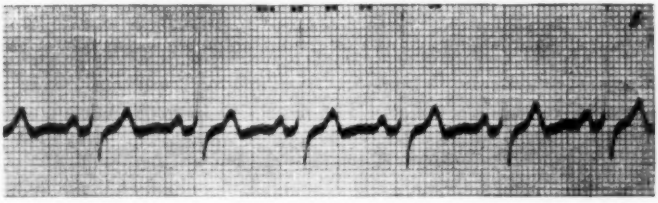

FIG. 8.—March 6. P–R = 0.18 second. Curve has practically returned to normal.

FIGS. 5, 6, 7 and 8.—Series of records from a case of bronchopneumonia with recovery, showing the electrocardiographic evidence of thorough digitalization and its long persistent effect.

increase in the heart-rate in the fatal cases was identical whether the subjects were thoroughly digitalized or had received no digitalis during their entire illness. No difference could be noted in the two series in the behavior of the blood-pressure. Daily observations by the auscultatory method were made of systolic and diastolic pressures in many cases. As a rule both systolic and diastolic pressures were low and the pulse-pressure showed a normal range. The level for each of these became established early in the disease and remained remarkably constant throughout the whole course, except that in the fatal cases a terminal rapid lowering of systolic pressure and a diminution in the pulse-pressure appeared to be the rule. Digitalis had no influence on the blood-pressure.

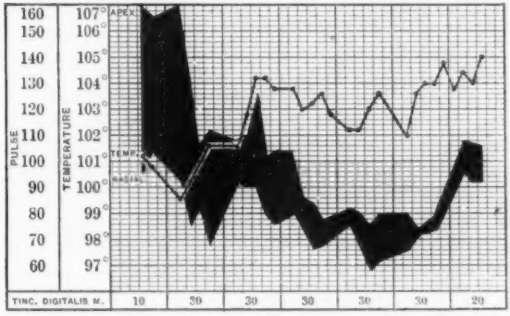

FIG. 9.—Chronic cardiac valvular disease with auricular fibrillation complicated by bronchopneumonia. Terminating fatally. Moderate doses of digitalis control the heart-rate which becomes relatively slow in spite of the high temperature and severe toxemia. The upper edge of the shaded area indicates the heart-rate counted at the apex by auscultation. The lower edge of the shaded area indicates the rate of the radial pulse. The shaded area indicates the pulse deficit.

FIBRILLATION. Among the cases of our series there were two instances of chronic cardiovascular disease with auricular fibrillation. These had certain points in common and presented evidence in regard to the action of digitalis which it is of interest to note. Both these men had been former patients in the Presbyterian Hospital and had been carefully studied. Both had had frank attacks of acute rheumatic fever followed by mitral stenosis and insufficiency and auricular fibrillation. During their former treatment in the hospital each had responded to the administration of digitalis in a satisfactory manner and had been discharged, with reasonably efficient hearts. During the epidemic these patients were readmitted with signs of patches of consolidation and presented typical pictures of the pneumonias seen in other numbers of this group, with the additional signs of cardiac insufficiency. In these cases digitalis was administered at once and continuously. In one the heart-rate, which on admission was 150, fell to 80 after

the administration of 175 minims of the tincture; the other had been taking digitalis before admission, but in spite of this the first observation showed a heart-rate of 160 and a pulse deficit of 64. The exhibition of 100 minims of the tincture of digitalis reduced the heart-rate to 80, with a deficit of 10 (Fig. 9). In each instance the circulatory condition was much improved, the heart became slow and appeared reasonably efficient. However, the temperature continued high, the overwhelming toxemia dominated the picture and the fatal termination came for one on the sixth and for the other on the tenth day of his pneumonia. In neither case was heart failure the apparent cause of death.

Cases of this nature illustrate the fact that in certain cases of auricular fibrillation digitalis acts promptly and efficiently in reducing the ventricular rate even in the presence of extensive consolidation and extreme intoxication.

Block. Our studies lead us to believe that digitalis had the same effect on the hearts of this series as in a similar group without pneumonia. In four instances out of several hundred in which digitalis was given there were found clinical and electrocardiographic evidences of partial heart-block which can only be attributed to the digitalis. One patient on admission presented a coupled rhythm and partial block. On inquiry we elicited the information that he had received six doses of strophanthin and digipuratum every six hours for some days. These drugs had been given subcutaneously, but the exact amounts could not be ascertained. Another who on his first examination showed an arrhythmia which was proved on electrocardiographic examination to be a partial block had been taking considerable doses of the tincture.

A nurse in the training school, aged twenty-six years, admitted on the first day of pneumonia with a perfectly normal heart, showed an arrhythmia due to a partial heart-block on the fourth day of her disease after the administration of 230 minims of the tincture of digitalis. She had a mild pneumonia with an uneventful course defervescing on her sixth day. Electrocardiographic records taken on the first day the arrhythmia was discovered and six days after the administration had been stopped are shown in Figs. 10 and 11. The two records show the characteristic effects of digitalis. The P–R interval is prolonged and of variable duration; occasionally there is a blocking of the impulse from the auricle. The T wave is characteristically altered.

Another case of our series was a man, aged twenty-five years, who had a very severe but uncomplicated pneumonia of the type usually seen in this series. Although his heart never appeared to be embarrassed, he was given from the first large doses of the tincture of digitalis. When this had totalled 465 minims a partial heart-block appeared. In Figs. 5, 6, 7 and 8 are presented a series of his electrocardiographic records, selected from those taken

at very frequent intervals, which show the characteristic changes of cardiac digitalization and the return of the heart activity to the normal. All four of these patients, showing block following digitalis, recovered and gave no evidence of subsequent ill effects from its administration. We were never able to discover any evidence that the heart of any one of these patients was abnormal. In this connection, however, it is interesting to note the response of different apparently normal hearts to the administration of digitalis.

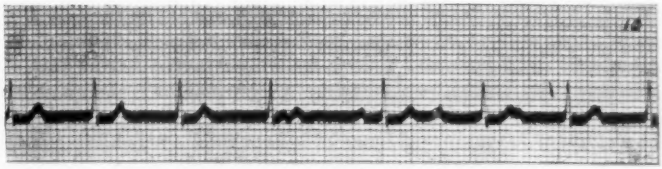

FIG. 10.—January 7, after tincture of digitalis 230 minims. Partial *A–V* block. *P–R* (variable) = 0.2+ second. No digitalis after this.

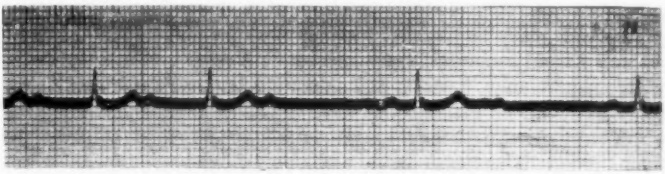

FIG. 11.—January 13. Partial block persists. *P–R* (variable) = 0.20 to 0.40 second.

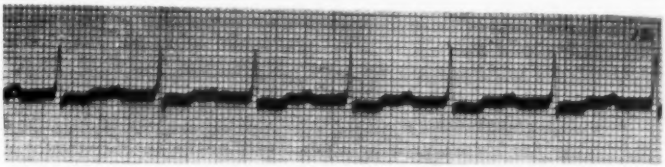

FIG. 12.—January 23. No digitalis since January 7. *A–V* block has disappeared. *P–R* = 0.28 second. *T* wave has changed.

FIGS. 10, 11 and 12.—Case of bronchopneumonia with recovery, showing partial block gradually disappearing after digitalis was discontinued.

In one case block appeared only after the administration of 465 minims of the tincture, in another an almost identical cardiac activity appeared after the administration of 230 minims of the tincture. The first was a man who weighed twenty pounds more than the second patient, who was a woman. There were other patients in our series who received considerably larger amounts of digitalis than the ones now under consideration, and yet showed no evidences of heart-block. With these variations in mind it seems to me it is wiser, unless the need is very urgent, to give

digitalis in moderate amounts and to approach complete digitalization gradually rather than by the use of the enormous initial doses that have been advised by some enthusiastic clinicians. Here, as in other fields of medicine, it is important to individualize, and it is unwise to administer digitalis by arbitrary fixed rules calculated on weight alone.

Chronic Valvular Heart Disease. In our hospital series there were thirteen who on admission presented the evidences of chronic cardiac valvular disease; all showed defects of the mitral valves; 11 were cases of mitral stenosis, with or without mitral insufficiency; 2 showed mitral insufficiency only. As might be expected all the members of this group showed a greatly accelerated heart-rate. With the exception of one man, who died eighteen hours after admission, all of these patients were effectively digitalized. None of them gave any evidence of a beneficial effect of the drug except the two cases with auricular fibrillation, which have already been described; these showed a marked slowing in rate, diminution in the pulse deficit, improvement in the quality of the heart sounds and a distinct betterment in the volume and quality of the pulse; in none of the others could any of these results be secured. Of the cases of mitral stenosis 2 recovered and 9 died. Of the cases of mitral insufficiency 1 recovered and 1 died.

Summary. The evidence here presented indicates:

1. That individuals with chronic cardiac valvular disease withstood the toxemia of the pneumonias of this epidemic very badly.
2. That individuals with normal hearts, who developed pneumonia, did not ordinarily die from cardiac insufficiency, and the postmortem examinations offer no proof that these hearts were essentially damaged.
3. That digitalis acts on the cardiac apparatus of these pneumonias in the same manner as in a similar series of hearts without complicating pneumonias.
4. That digitalis reduced the heart-rate only in cases of auricular fibrillation and in cases where it was administered in quantities sufficient to produce an actual auriculoventricular block.
5. That the administration of digitalis did not influence blood-pressure.

In view of the apparently widespread belief that death in pneumonia is usually due to heart failure and the almost universal dependence that is placed on digitalis in this condition, it behooves us to examine critically the fragments of evidence which we have been able to accumulate in the recent epidemic.

The employment of a method directed against a wrong conception of the pathology may lead to a false sense of security and keep us from directing our efforts to secure remedies better fitted to combat the true pathological condition.

TRANSFUSION OF BLOOD IN PERNICIOUS ANEMIA: REPORT OF AN INTERESTING CASE.*

By J. M. Anders, M.D., LL.D.
PHILADELPHIA.

This paper is not an attempt to solve the problem of the genesis of pernicious anemia, although some of the views bearing on this phase of the subject are briefly discussed. Neither can it be claimed to offer anything novel by way of treatment. The chief aim has been to validate the claim advanced by certain writers that transfusion offers more for progressive pernicious anemia than any other form of treatment, by a survey of the clinical results obtained principally by surgeons during the decade last past, Werner Schultz[1] having given a complete bibliography up to 1910.

Some of the gaps in our knowledge of this obscure disease promise to be filled from the field of comparative pathology. For example, Seyderhelm[2] has demonstrated that injected extracts of the larvæ of the fly, *Estrus equi*, which is found in the walls of the horse's stomach, produce symptoms characteristic of the severer types of anemia.

Seyderhelm has also shown that the hemolytic lipoids derived from the fly larvæ do not cause the symptoms of severe anemia, but rather the non-hemolytic fragments of larval substance.

If the foregoing view be correct the theory of defective hemogenesis, which is held by Henry, Rindfleisch, MacKenzie and other hematologists as the primary cause of pernicious anemia, cannot be altogether abandoned, although injury to the hematopoietic organs, so far as scientific evidence is concerned, occupies a less conspicuous place in the etiology of this disease than toxic hemolysis. It would appear to be clear that the blood picture presented by pernicious anemia reflects an effort of the blood-generating organs to compensate the unusual hemolytic activity of unknown origin. In this connection the abnormally large pigment depositions to be found, more particularly in the liver and spleen, at necropsy in this disease, confirm the highly fatal blood destruction which characterizes the complaint. The fact that defective lipoid metabolism results in diminished hemolytic properties of the whole blood should be also recollected.

Additional evidence of the pernicious activity of hemolytic agents in Addisonian anemia is afforded by the presence of an undue quantity of urobilin in the stools. Moreover, Sellards and Minot[3] have

* Read before the Association of American Physicians, Atlantic City, June 16, 1919.
[1] In Crawitz, Klinische Pathologie des Blutes, Leipsic, 1911, p. 381.
[2] Arch. f. exper. Path. u. Pharmakol., 1918, lii, 253.
[3] Jour. Med. Research, 1916, xxxlv, 469.

shown that hemoglobinuria follows the subcutaneous injection of hemoglobin in amounts incapable of producing the appearance of urinary blood pigment in other types of anemia. Eppinger[4] contends that the excessive erythrocytic destruction, which takes place in the spleen (the exact site of the hemolysis being the splenic pulp) is due to the anatomical changes presented by this organ in pernicious anemia. In those anemias of the pernicious type, which are due to known causes, *e. g.*, malignant tumors, "hemolytic toxins are possibly responsible for the blood condition" (Kullmann[5]), Krehl[6] and others direct attention to an increased regeneration of erythrocytes in pernicious anemia, which accounts for the escape of immature red cells, including the characteristic megaloblasts, into the circulation.

Sajous[7] states that hemolysis occurs whenever toxics, either endogenous or exogenous, appear in the blood in quantities sufficient to excite a defensive reaction. He continues: "The antibodies then attack not only the toxics but the erythroctes as well." H. A. Christian[8] concludes that in severe cases of Addisonian anemia the renal function is disturbed much as in advanced chronic nephritis. This seems to be either a toxic or nutritional disturbance in renal cellular activity.

On the basis of modern researches and sound data, prophylactic measures are attracting professional attention, after ascertaining the presumable etiological factor in the given case. For example, certain observers attach prime importance to oral sepsis as the cause of the disease; this, however, produces a secondary type of anemia. L. F. Barker and G. P. Sprunt[9] have emphasized this phase of the problem, recommending the removal of all discoverable foci of infection; they further advise an abundant, roborant diet, arsenic, the exhibition of hydrochloric acid immediately after meals and of pancreatin and calcium carbonate three hours after each meal. I have mentioned the main details because of their claim that under this treatment splenectomy and transfusion of blood were not found necessary in a special group of cases.

Leyton[10] affirms that massive transfusions of blood offer the greatest chance of improvement to sufferers from pernicious anemia, but, he adds, "Any error in the technic may be followed by a fatal result." Archibald[11] transfused a series of 20 cases at the Mayo Clinic, with marked immediate benefit in 69 per cent., while among 14 cases deemed unsuitable for splenectomy similar improvement was noted in 50 per cent. Vogel and McCurdy[12] regard the transfusion of physiologically unaltered blood as a palliative treatment

[4] Berl. klin. Wchnschr., 1913, c, 2409.
[5] Ztschr. f. klin. Med., p. 3.
[6] The Principles of Clinical Pathology, p. 148, Philadelphia.
[7] Index Supplement, p. 133.
[8] Arch. Int. Med., October, 1916.
[9] New York Med. Jour., June 9, 1917.
[10] Practitioner, London, March, 1917.
[11] St. Paul Med. Jour., February, 1917.
[12] Arch. Int. Med., 1913, xii, 707.

of great promise. Kimpton,[13] who transfused upward of fifty cases, is of the opinion that transfusion offers more for this disease than any other form of treatment.

It is highly probable, at least, that transfusion of blood in this disease owes its beneficial effects principally to stimulation of the antihemolytic properties of whole blood, although possibly also to some extent to its power to increase the activity of the bone-marrow. Obviously, anything that will tend to evoke a strong defensive reaction against the special hemolytic factors will prove useful.

Turk,[14] however, believes that the added blood, combined with some putative hemolytic present, thus protecting the bone-marrow, allows it opportunity to retrieve some of the lost cells.

Case Report.—A. F., aged sixty five years, retired merchant, of healthy parentage began to decline in health about March 1, 1918, growing weak and pale as well as dyspneic. Anorexia soon was complete, and there were belching, abdominal distress, a tired, languid feeling, loss of physical strength and marked mental hebetude.

On physical examination nose, throat, eyes, ears normal; had several decayed teeth which were extracted. There was a marked mitral murmur. May 1, 1918, went to Atlantic City for three weeks, but became progressively weaker during his stay there, so that he had to be removed to his home, not being able to move about without assistance.

May 19, blood count showed: Hemoglobin, 20 per cent. (von Fleishel); erythrocytes, 720,000; leukocytes, 3400. Differential count: polymorphonuclear neutrophiles, 72 per cent.; small lymphocytes, 23 per cent.; large lymphocytes, 2 per cent.; transitional, 2 per cent.; mast-cells, 1 per cent.

Marked anisocytosis and poikilocytosis; megalocytes predominate; polychromatophilic degeneration; very few erythroblasts.

Upon this laboratory evidence and the clinical symptoms and course pernicious anemia was diagnosed. I was called to see the patient May 22 by the attending physician, Dr. S. Shaham, concurred in the diagnosis and gave an unfavorable prognosis, based upon the patient's feeble condition. Transfusion was performed May 24 by Dr. A. J. Rubenstone, 500 c.c. of whole blood from the patient's son, which was found compatible by the Roux-Turner method, being transferred. This was followed later in the day by slight chill, rise of temperature to 102° F., and marked restlessness, from which the patient quickly recovered after injecting several doses of adrenalin chloride and atropin. Rapid clinical improvement followed; color improved markedly, patient asked for food, and within one week he was out of bed.

[13] Boston Med. and Surg. Jour., May 14, 1918, No. 11, clxxviii, 351.
[14] Vorlesungen über klin. Hamatologie, Vienna, 1912.

Author.	Reference.	Number of cases.	Number of transfusions.	Method.	Results.	Remarks.
L. H. Hemplemann	Int. Med. Jour., 1910, xvii, 316	1	1	Direct transfusion	"Improvement lasting a short time."	
A. M. Fauntleroy	U. S. Naval Med. Bull., 1911, v, 47	2	4	Vein to vein	Temporary remissions.	
O. Hannsen	Verhandl. d. Cong. f. inn. Med., 1911, xxviii, 141	14	45	Intravenous injection of defibrinated blood	Remissions in 8 cases; doubtful benefit in 2 and none in 4	First transfusion at times negative; later ones effective.
E. Elliot, Jr.	Ann. Surg., 1911, liii, 131	1	1	.....	Remission over 2 months.	
G. Woolsey	Ann. Surg., 1911, liii, 131	2	2	Artery to vein	Decided remission in 1 case; other sl. improved	First case infected with malaria.
J. A. Hartwell	Med. Rec., 1911, lxxvii, 1005	1	4	.....	Remissions lasting a few weeks.	
D. Bovaird, Jr.	Med. Rec., 1911, lxxix, 239	3	3	Direct transfusion	Remissions in 2	Malarial infection resulted in 1 case.
Bennecke	München. med. Wchnschr., 1912, lix, 1571	4	4	Vein to vein	Negative	All in terminal stage.
B. M. Bernheim	Jour. Am. Med. Assn., 1913, lxi, 268	2	5	.....	1. Repeated remissions; 2. Negative.	
H. M. Vogel and U. F. McCurdy	Arch. Int. Med., 1913, xii, 707	4	7	.....	Temporary remissions after first injections.	
E. Lindemann	Jour. Am. Med. Assn., Mar. 28, 1914	19	40	.....	11 remissions; 8 unimproved.	
A. H. Noehren	Buffalo Med. Jour., 1914–15, lxx, 347	1	1	.....	Died 11 days after transfusion.	
R. Ottenberg and E. Libman	Tr. Assn. Am. Phys., 1915, xxx, 149	25	32	.....	Remissions in 14 cases, 11 not benefited; duration: 1, 3 mos., 3, 6 or more mos.; 3, a year or more; 3, over 2 years.	
J. H. Gibbes	South. Med. Jour., 1915, viii, 48	1	2	.....	Remission.	
W. V. Brem	Jour. Am. Med. Assn., July 15, 1916, p. 190	24	82	Citrated	.....	Reaction in 25 per cent.; 1 patient received 20 transfusions.
J. W. Churchmann	Jour. Am. Med. Assn., Sept. 9, 1916	1	Several	.....	Marked remission	
F. W. Birtch	California State Jour. Med., June, 1916, p. 240	2	..	.....	1 remission	Developed syphilis from son.

H. E. Mileny, W. W. Stearns, S. G. Fortuine, R. M. Ferry	Am. Jour. Med. Sc., 1917, cliv, 733	40	164	Both citrated and whole blood	"Spontaneous remissions definitely hastened in many cases."	
H. Z. Giffin	Jour. Am. Med. Assn., Feb. 10, 1917, p. 429	19	..	.....	Marked gain in 8; sl. in 6; no improvement in 4	Transfusions were preparatory to splenectomy.
R. D. McClure and G. R. Dunn	Johns Hopkins Hosp. Bull., Mar., 1917, p. 99	17	64	.....	Beneficial, 53 per cent.; no benefit, 35 per cent.; harmful, 10 per cent.	7 to 10 per cent. gave reactions.
A. E. Stamfeld	Lancet, London, March 31, 1917, p. 484	9	..	.....	Marked remissions in 4; less marked in 3.	
R. G. Larabee	Boston Med. and Surg. Jour., April, 1917, p. 553	6	8	.....	Remissions in 4 cases lasting from 2 to 11 months.	
C. R. Minot and R. I. Lee	Boston Med. and Surg. Jour., 1917, clxxvii, 761	46	89	.....	Marked remissions in 9; definite but slow in 20; 17 unimproved	Reactions followed 34 transfusions.
C. G. Heyd	New York Med. Jour., 1917, cvi, 57	1	1	.....	No remission.	
V. P.W. Sydenstricker, V. R. Mason, and T. M. Rivers	Jour. Am. Med. Assn., June 9, 1917, p. 1677	11	49	Citrated.		
O. Leyton	British Med. Jour., April 1, 1916, p. 484	1	2	.....	Remission after first transfusion.	
A. Archibald	St. Paul Med. Jour., 1917, xix, 43	26	46	.....	61 per cent. received distinct benefit.	
C. K. P. Henery	Canadian Med. Assn. Jour., 1917, vii, 18	2	..	.....	1 slightly improved; 1 negative.	
E. L. Goar	Texas State Jour. Med., Mar., 1918, p. 388	1	1	Whole blood	Temporary remission.	
V. C. Hunt	Texas State Jour. Med., Sept., 1918, p. 192	123	403	Citrated	Marked remissions in about 60 per cent. with reactions; poor response in 40 per cent. in absence of reactions	Reactions in 94, or 23 per cent.; poor response when no reaction.
E. Schisler	Jour. Missouri State Med. Assn., 1918, xv, 192	1	3	Citrated	Improvement.	
A. Bloomfield	Johns Hopkins Hosp. Bull., 1918, xxix, 101	26	.	Mostly citrated	Remissions in 51 per cent.; average duration 5½ mos.	
S. W. Sappington	Hahnemann Monthly, Philadelphia, 1918, liii, 518	13	19	Citrated	Majority developed remissions lasting several mos. up to 16 mos.	
S. Shaham and J. M. Anders	Not published	1	2	Whole blood	2 remissions.	Last remission still holding.
		450	1084			

June 3, 1918. The patient had resumed his normal activities and a blood count now showed: Hemoglobin, 40 per cent; erythrocytes, 2,050,000; leukocytes, 5400. Differential count: polymorphonuclear neutrophiles, 57 per cent.; small lymphocytes, 34 per cent.; large lymphocytes, 4 per cent.; transitional, 1 per cent.; mast-cells, 1 per cent. Some anisocytosis; megalocytes predominate; some poikilocytosis.

The cardiac murmur had entirely disappeared and improvement from then on was steady. Arsenic and iron injections hypodermically, which he had received since transfusion every other day, were now suspended. The patient was next seen November 19, 1918, and appeared perfectly well. Indeed, he stated that he had "not felt so good for fifteen years."

November 19. Blood count: Hemoglobin, 70 per cent.; erythrocytes, 3,280,000; leukocytes, 5000. Differential count: polymorphonuclear neutrophiles, 63 per cent.; small lymphocytes, 37 per cent.; some anisocytosis and megalocytosis. The patient continued to do unusually well until January 1, 1919, when he slowly developed a relapse. A little pallor, a little cardiac palpitation, dyspnea and anorexia, appeared.

The blood count January 23 showed: hemoglobin, 60 per cent.; erythrocytes, 1,700,000; leukocytes 3600. Differential count: polymorphonuclear neutrophiles, 72 per cent.; small lymphocytes, 26 per cent.; large lymphocytes, 2 per cent. Megalocytosis, reds stain intensely.

March 8. Transfusion repeated. Almost no reaction followed, but improvement was immediate, although somewhat slow and gradual. He has now, May 15, 1919, returned to the same state that he presented in November, 1918. Blood count: hemoglobin, 65 per cent.; erythrocytes, 3,160,000; leukocytes, 6000. Differential count: polymorphonuclear neutrophiles, 62 per cent.; small lymphocytes, 33 per cent.; large lymphocytes, 3 per cent.; transitional, 2 per cent. Patient's general condition is now remarkably good, just one year after the first transfusion, being able to attend to duties that he has not performed for the past ten years.

It was the surprisingly brilliant result obtained in this case, that impressed me with the need for a careful survey of the recorded experiences of clinicians and surgeons with this procedure during the decade last past. The accompanying table sets forth the main results of my collective investigations.

The totality of 450 cases, in which 1084 transfusions were performed, is large enough to base thereon a fairly accurate estimate of the value of transfusion as a remedial measure. Considerable light has been thrown upon the question of the duration of remissions by transfusion by these observations, although the reports are too often silent on this phase of the effects of the procedure. Of 362 cases in which the result was given, 204, or 56.3 per cent., showed

an initiation of remissions. Cases in which the improvement was brief and might have been ascribable to the mechanical effects of the transfusion were not included in the figures representing remissions. It is worthy of note that the average number of transfusions per patient was 2.4, while the extremes ranged from 1 to 20 operations.

Weber,[15] Hurter[16] and others have, as a result of personal observation, reached the conclusion that repeated smaller transfusions, *e. g.*, "200 to 500 c.c.," which are free from dangerous reactions, give more satisfactory results than single, massive ones. The series of cases which make up the accompanying table confirm this view. Single transfusions, however, prove sufficient in a certain percentage of cases (11 out of 26, Archibald). The determination of the precise amount of blood to be transferred is a question requiring further study and investigation. Of 185 cases in which the method was mentioned, 172 were transfused with citrated blood.

In this connection Vogel and McCurdy conclude, as the result of their studies that "The enumeration of the reticulated cells by means of the method of vital staining affords a useful means of gauging the hemopoietic activity of the bone-marrow, and by watching the patient's progress in this way the indications for and effects of various therapeutic measures can be well determined and supervised." The intervals in the case of multiple transfusions, must be determined by repeated examinations of the patient's blood, preferably by the method of Vogel and McCurdy, since this is the only trustworthy method of estimating their effect. Obviously, the patient's general condition and subjective sensations must likewise be taken into account.

The splendid results achieved from transfusions by a large number of excellent observers, in an innately fatal disease in which the diagnosis cannot be said to be conjectural, except at an early stage, render it highly expedient to determine their precise field of usefulness. Shall they be employed so soon as the diagnosis of the disease can be made with accuracy in progressive cases? or shall they be limited to the cases that have proved refractory to the arsenical treatment including salvarsan and neosalvarsan, "with results that promise their continued use as the most certain form of therapy in this disease?"[17]

It is believed by a number of competent observers, *e. g.*, Bovaird,[18] Lee, Minot and Vincent,[19] Ottenberg and Libman,[20] and others that when the hemoglobin percentage falls to or below 20 per cent. transfusion of blood offers the possibility not only of averting death;

[15] Deutsch. Arch. f. klin. Med., 1909, xcvii, 165.
[16] Med. Klin., 1911, No. 12.
[17] Da Costa's Handbook of Medical Treatment, ii, 21.
[18] Medical Record, February 11, 1919.
[19] Jour. Am. Med. Assn., September 2, 1916, p. 719.
[20] Am. Jour. Med. Sc., July, 1915, p. 36.

but at times at least of initiating one of the periods of quiescence so characteristic of the disease.

That it is unwise to wait until the average hemoglobin percentage falls as low as 20 per cent. is a conclusion supported by both clinical experience and statistical evidence. Ottenberg and Libman[21] found that the average hemoglobin percentage before transfusion of 14 cases which showed remissions was 27 per cent., "whereas the average of 9 cases which show no remissions (excluding rapidly fatal cases) was only 20 per cent.

In the case which had reached an advanced stage before the procedure was resorted to, briefly reported above, the effects of the first transfusion were decided and lasted about eight months, and a second transfusion gives promise of an equally favorable result. As a means of establishing a reputation for the procedure, however, the limitation of its use to well-nigh hopeless cases is not promising. The present researches indicate clearly that earlier transfusions in cases showing no tendency to spontaneous remission or as the result of the more usual methods of treatment would yield the best results. Again, remissions are more easily induced in the earlier than the later stages of the disease.

Transfusion does not prolong the period of remission. Cabot's figures show the quiescent period to be over 6 months in 165 out of 329 cases, whereas in my series, so far as could be ascertained from available literature, it was somewhat shorter on the whole. On the other hand, this measure easily brings about an increased number of remissions, hence it is not unreasonable to suppose that the total duration of life may be thereby prolonged, as was doubtless the case in many instances included in my table. Evidence exists to show that those examples of the disease which have shown most improvement after transfusion had run a prolonged course as a rule, while the more rapidly progressive cases manifested a feebler remission.

Two methods of administration of defibrinated blood—namely, by intramuscular and intravenous injection—have been advocated, but the results are less satisfactory than those yielded by whole blood. Curtis and David,[22] after making experiments on dogs, consider defibrinated blood unsuitable for human transfusion and Pike, Guthrie and Stewart,[23] and others have found that defibrinated blood on standing a few hours undergoes changes affecting the corpuscles and impairing its nutritive and bactericidal qualities. In view of these facts, and remembering that fresh unaltered blood can, thanks to the recent advances in vascular surgery, be safely transferred from one individual to another, the further use of defibrinated blood is rendered quite undesirable.

It has been suggested to employ antidiphtheria serum in those examples of the disease in which the toxemia predominates and

[21] Loc. cit.
[22] Surg., Gynec and Obst., 1912, xv, 476.
[23] Jour. Exper. Med., 1908, p. 371.

counteracts the action of the arsenic. It seems to me, however, that in many of these cases more favorable results would be obtained from the injection of whole blood after combating discoverable causes. The same remark applies to venesection which has been advised as a palliative measure. Other special methods of treatment have been employed in cases refractory to arsenic and iron therapy, *e. g.*, by the hypodermic use of splenic extract (Maikhailoff) and antistreptococcus and antistaphylococcus serums; but these have not gained an enviable reputation for themselves, and it is unwarrantable to permit them to supersede transfusion of blood, which deserves a more extended trial and promises a far better therapeutic effect.

From an examination of the available literature and personal observation and knowledge of individual cases, I concur in the opinion expressed by Kimpton that the results of splenectomy hardly warrant the operation. This view is based on the assumed facts that transfusion offers quite as much as splenectomy, "with or without transfusion"(Kimpton), and that it obviates immediate deaths. The belief among certain observers that transfusion following splenectomy brings a more steady response than without splenectomy is not borne out by professional experience as a whole.

Krumbhaar,[24] in a series of the late results of splenectomy in 153 cases, noted a mortality rate of about 20 per cent., and also that, as a rule, the improvement was transient. Moffitt,[25] in an earlier article, states that of 33 cases of splenectomy for pernicious anemia gleaned from the literature, including one under his own observation, "eight died immediately or not long after the operation."

It is obvious that a method of so great promise as transfusion should be more widely adopted as a means of prolonging life. Berheim[26] has reported the interesting case of a man admitted to the clinic of Dr. J. C. Bloodgood, who was transfused four different times from three donors and lived two years after having been given up as lost. In the small percentage of cases in which severe and increasing reactions follow the use of homologous blood, the injections should be discontinued.

Since the technical success of the operation in competent hands is assured, both as regards the recipient and donor, it should be repeated with sufficient frequency to avoid the development of an extreme degree of anemia.

The question arises, Have we not arrived at the point at which internists and general practitioners, under whose observation and care pernicious anemia first falls, as a rule, should advise immediate transfusion after an assured diagnosis has been made, during the non-quiescent period, seeing that it initiates a prompt remission in at least 56 per cent. of the cases? This procedure should be,

[24] Jour. Am. Med. Assn., 1916, lxvii, 723.
[25] Am. Jour. Med. Sc., No. 6, cxlviii, 822.
[26] Jour. Am. Med. Assn., 1913, lxi, 268.

however, supplemented by appropriate hygienic measures and approved medicaments, and in cases which are refractory to transfusion the usual medical treatment by arsenic, including salvarsan intravenously, and subcutaneous injections of iron, should receive a trial before resorting to other methods of treatment. Finally, the dictum that this measure, when skilfully employed, offers more than any other method of treatment alone, is confirmed by the results of my collective studies.

My sincere thanks are due Dr. S. Shaham, for permission to publish the report of his interesting case, and also Dr. A. J. Rubenstone, for certain details connected with his two transfusions.

HYPERTENSION: ITS SIGNIFICANCE, RELATION TO ARTERIOSCLEROSIS AND NEPHRITIS AND ETIOLOGY.[1]

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Significance of Hypertension. The introduction of the sphygmomanometer has been of profound consequence to clinical medicine. It has helped to clarify our knowledge of many diseases associated with alterations of circulatory dynamics; it has introduced new concepts into clinical medicine, refined prognosis, made clearer our understanding of the action and benefit of certain drugs and has made our therapy of circulatory disturbances more subtle. At the same time there is no instrument of precision whose correct use is more commonly misapplied. This is especially true in relation to that group of disorders associated with "hypertension."

At the outset it must be emphasized that hypertension is not a disease but a symptom. The conception of a hypertension as a disease dates from the earlier years when the sphygmomanometer revealed an increase in blood-pressure in instances in which it was not distinguishable by the *tactus eruditus*. Viewing hypertension as a disease efforts were directed to reduce the blood-pressure at all hazards, so that the use of vasodilating drugs, especially those of the nitrite group, became a common custom. The view is now held that hypertension, instead of being an unmitigated evil, represents a compensatory process, brought about by the attempts of the circulatory apparatus to regulate the proper distribution of the blood volume. Certain it is that a high arterial tension is perfectly compatible with well-being, and is often discovered by pure accident. On the other hand it is a common occurrence to witness that both

[1] Read before the Clinical Conference, Mt. Sinai Hospital, New York City.

the subjective and objective phenomena of a condition associated with hypertension improve under treatment, although the blood-pressure, especially the systolic, has not been altered appreciably. Viewed in the light of a compensatory process, an increased arterial tension bears an entirely different significance. In the strictest sense of the word, therefore, a circulation in which a high arterial tension is an element is in a state of decompensation; that is, its maximum efficiency is to a certain extent impaired. There is much confusion in the minds of most authorities as to what we understand by the term "decompensation" in cardiac disorders, probably for the reason that we do not understand the exact forces that bring decompensation about. In our minds "decompensation" connotes the graver signs and symptoms of cardiac disease, such as breathlessness, aggravated forms of cardiac rate and rhythm, anasarca, etc. But, strictly speaking, any deviation from the normal represents a state of circulatory decompensation, and these deviations may refer to both subjective and objective phenomena.

Subjectively the patient's complaints may vary from a slight fatigue or breathlessness or occasional mild headache to the severe inertia, panting and splitting vertex headaches of the advanced nephritic. Objectively the patient may reveal a gamut of signs varying from simple hypertension to the profound circulatory disturbances of advanced cardiac disease. Moreover my observations lead me to conclude that the subjective and objective phenomena of decompensation represent a progressive process, and that every persistent hypertension, unless complicating factors are introduced, will eventually result in the graver evidences of decompensation represented under the conventional clinical picture of cardiac insufficiency. This suggests the following theorem: *Every patient in whom a persistent hypertension is found requires not only observation but treatment; and the form of treatment depends upon how far we are able to restore the patient's condition, both subjectively and objectively, to the normal.* I emphasize both terms, subjectively and objectively, because I have seen not infrequently patients in whom the subjective symptoms were almost completely relieved, although the objective findings were not appreciably altered. It will be found in the vast majority of instances that treatment will restore compensation up to a certain point beyond which we cannot pass. It has often been asserted that a circulation associated with a hypertension even of a considerable degree can never be restored to the normal. But I am convinced that this statement is not correct. I know of a number of instances in which hypertension, associated with the usual subjective and objective phenomena, such as breathlessness, fatigue, headache, oliguria, albuminuria, etc., has disappeared completely and thus far remained absent.

Varieties of Hypertension. Much has been written of late of "essential" hypertension or "hyperpiesis," By these terms we

refer to cases in which hypertension is manifest with a left ventricular hypertrophy, but without any appreciable clinical evidences of kidney or arterial disease. Indeed, such cases have come to autopsy and no disease of the arteries or the kidneys has been found. Recognizing, however, that hypertension is known to occur with outspoken clinical and pathological evidences of arteriosclerosis and kidney disease, clinicians have attempted to classify hypertension from the standpoint of etiology, therefore, into three distinct types: (1) Arteriosclerotic; (2) nephritic; (3) essential. The fallacy of this classification is that it attempts to explain etiology in terms of pathological anatomy. Because a certain pathological lesion is found at postmortem is no proof whatever that this lesion was the cause of the signs or symptoms during life. A lesion may very well be the end of a physicochemical or metabolistic process which is not demonstrable at the autopsy table. It would be equally logical, for instance, to conclude that the left ventricular hypertrophy or an apoplexy is the cause of the hypertension, although we know that these lesions are the result and not the cause. Furthermore, such a classification does not take into consideration the fact that the status of the patient either clinically or at the postmortem table represents simply a phase of the disease and not a complete end-result. We are all familiar with cases of so-called essential hypertension which after several years have developed all the graver manifestations of kidney or arterial trouble. Indeed, I question whether every case of essential hypertension, unless cut down by some intercurrent malady, will not eventually develop signs of advanced kidney or arterial disease. All the evidence seems to show, as I shall shortly elucidate, that the majority of the so-called arterial and kidney diseases which have hitherto been regarded as the causes of hypertension are rather the result of hypertension rather than the the cause, and that therefore the terms "essential" hypertension, "arteriosclerotic" hypertension and "nephritic" hypertension are phases of one and the same process rather than three sharply defined clinical entities. A concept based upon this thesis will, I believe, help to eliminate much of the confusion in current writings of the subject. I therefore shall try to show that many, perhaps the vast majority, of so-called types or varieties of hypertension begin as simple "essential" hypertensions, and that eventually, after a sufficient lapse of time, such "essential" hypertensions assume the clinical form of "arteriosclerotic," "nephritic" and other hypertensions.

This classification, I repeat, is not etiological but clinical and teleological, and is of value only as emphasizing the organ or organs more prominently affected in the course of the disease and the immediate cause of death.

Such a classification, moreover, is incomplete, because it emphasizes only two of the organs that are affected in hypertension,

namely, the arteries and the kidneys. Now, hypertension is a malady that affects the circulation and therefore the function of all of the internal organs, and because of their critical function, the heart, the brain, the aorta, the arteries and the kidneys stand out prominently. Clinical manifestations involving one or more of these organs reveal themselves in every case of hypertension at one phase or other of the malady, so that a complete classification would include not only the nephritic and arteriosclerotic types, but the cardiac, cerebral and aortitic types as well. Such a classification would bear the additional merit of conforming to the three main kinds of death that come to such patients: (1) Cerebral (apoplexy); (2) cardiac (insufficiency, coronary disease); (3) nephritis (uremia). Why a hypertension should emphasize the lesion in one or the other organ is a problem that is at present not understood. In most instances, indeed, it is difficult to determine which organ is more severely affected.

I am not willing to assert at this time that all hypertensive states begin as cases of essential hypertensions. I shall discuss the conditions under which a hypertension may be secondary in a subsequent part of this paper. This question has given rise to two great problems that have been vexing those interested in the subject: (1) The relation of hypertension to arteriosclerosis; (2) the relation of hypertension to nephritis.

1. *The Relation of Hypertension to Arteriosclerosis.* The fact that hypertension occurs, as a rule, at that time of life when sclerotic lesions in the arteries become prominent has led many to believe that the sclerotic changes are the cause of the hypertension. But there is no fact more easily demonstrable in every autopsy room than that profound sclerotic changes may be manifest without the slightest evidence of hypertension during life (senile or decrescent type of Allbutt), and conversely that an extreme hypertension may have been present with little if any changes in the bloodvessels. Indeed, there is no relationship whatever between the extent of the arteriosclerosis and the height of the blood-pressure.

Whatever experimental evidence we possess seems to show that arteriosclerosis, sometimes at least, is the result and not the cause of a continuous state of hypertension. The frequency of arteriosclerotic lesions in animals after repeated injections of such blood-pressure raising substances as adrenalin, nicotin, barium chloride, etc., are well known; more convincing, because a direct toxic effect is eliminated, are the experiments of Harvey and Klotz, who maintained a continuous hypertension in young animals by placing them in an inverted position for three minutes over a period of 120 days, at the end of which time marked sclerotic changes in the bloodvessels were manifest. As further evidence of the direct effect of pressures on the formation of arteriosclerosis, we cite the well-known observations that atheroma is especially common at those areas of the

arterial tubes in which pressures are greatest, such as "at bifurcations; at narrow points whether normal or morbid and at dilatations with change of wave leading to distortion and elongation" (Allbutt). In congenital stenosis at the site of ductus Botalli, for instance, the aorta on the proximal side and the carotids and the cerebral arteries are extremely diseased, while on the distal side the internal surface of the vessels is normal.

2. *Relation of Hypertension to Nephritis.* Here we are treading upon a far more debatable ground. It is admitted that in practically every case of hypertension, albumin, most often a trace, with or without casts, is present in the urine. The questions then to determine are the following: (1) Does the presence of albumin, with or without casts, represent real damage to the kidney in the sense of a nephritis? (2) What clinical criteria do we now possess that a nephritis is present in the anatomical sense? (3) If an anatomical nephritis is proved by autopsy, how can we determine whether it is primary or secondary? (4) Is a proved anatomical nephritis always accompanied by the changes of the urine, conventionally associated with the term "nephritis," namely, albumin and casts? (5) Is there any proportional relation between the amount of damage to the kidney and the urinary and clinical findings, with special reference to the degree of hypertension? (6) Is there any definite relation between either the presence or degree of hypertension to the three conventionally described types of nephritis, namely: (*a*) Glomerular nephritis; (*b*) parenchymatous nephritis; (*c*) interstitial or arteriosclerotic nephritis? In other words, does the presence or degree of hypertension depend upon the extent of damage to the glomeruli, the tubules or to the interstitial tissue with its containing bloodvessels? (7) Have we any demonstrable proof that a hypertension may occur without an anatomical nephritis? (8) What do we understand by the term "nephritis" in the pathological sense?

As the answers to these questions will, in a great measure, overlap each other, I shall discuss these matters rather freely.

In the first place, does the presence of albumin, with or without casts, represent real damage to the kidney in the sense of a nephritis? The answer, of course, is a decided "No." The best proof is the absence of any kidney lesion in cases of orthostatic albuminuria in which even large amounts of albumin, and occasionally even casts, are present, although the kidneys are normal. The greatest difficulty that arises in an attempt to settle this problem is the fact that a kidney absolutely free from some evidence of inflammation is rarely found at autopsy, especially in adults, in whom hypertensive states are most likely to occur. Pathologists permit themselves a very wide latitude in their interpretation of an inflammation of the kidney, and will include everything from a slight cloudy swelling of the tubules or a slight round-celled infiltration to the

grossest destruction of the kidney parenchyma. With such a latitude a perfectly normal kidney is an almost impossible phenomenon in the adult. On the other hand, every pathologist knows that the extent of a degenerative or interstitial process in the kidney is the worst kind of a guide as to the amount of albumin in the urine. It is not uncommon to see a slight degenerative change associated with an enormous quantity of albumin, while an intense and widespread degenerative and interstitial process, the so-called contracted kidney, for instance, is associated with mere traces. On the other hand, it is not at all uncommon to find even an intense chronic nephritis without any history of a persistent albuminuria during life. It is admitted that albumin, as discovered by the conventional clinical methods, connotes a pathological change in the organism. What then is the significance of albumin in the urine? The process of urinary excretion is exceedingly complicated and depends on many factors, many of which are still not closely understood (Cushny). However, in whatever light the function of the kidney may be viewed, albumin may arise in the urine as the result of one or more of the following factors: (1) A change in the colloidal constitution of the plasma permitting a greater diffusibility of albumin through the vessels; (2) degenerative changes in the kidney epithelium, with consequent alterations in filterability; (3) autolysis of kidney parenchyma, with solution of proteins into the urine; (4) bloodvessel changes, especially of the glomeruli, permitting albumin to escape more readily into the tubules; (5) static changes in the blood supply of the kidney, whereby intravascular and extravascular balances of pressure are disturbed.

The precise relation of these factors to the excretion of albumin in the urine has, as far as I am aware, not yet been formulated. I only wish to point out that the prevalent conception of albuminuria as being due wholly to a gross injury of the kidney parenchyma is, in my opinion, greatly exaggerated. I am willing to admit that this factor perhaps plays the largest role in the albuminuria of acute infections, in which changes, especially cloudy swelling, of the kidney epithelium is a prominent lesion; but I do not believe it is a factor of much consequence in the albuminurias associated with hypertensive states.

On the other hand, I believe that the last factor, namely, static circulatory conditions within the kidney itself, with or without vascular lesions, are the dominant causation of most of the albuminurias not associated with the infections. My interest was focussed on this phase of the problem many years ago. It happened as the result of one of those rare opportunities in being able to observe closely over a period of four years a case from its very inception to the autopsy, during which time practically all the clinical and urinary examinations were made by myself, so that my interpretation was not in the slightest degree biassed. The case was that

of an aged physician who suffered from attacks of cardiac decompensation (auricular fibrillation), as the result of an aneurysm of the left ventricle, brought on by coronary thrombosis. The patient felt perfectly well previous to his attack of coronary trouble, and his urine had always been normal. The blood-pressure was always normal. He was kept under the constant use of digitalis, to which he responded perfectly, so that in the intervals between his attacks of cardiac insufficiency he felt well. His pulse was slow and regular, and this is the point—*his urine was perfectly normal; there never was the slightest trace of albumin.* When, for any reason or other, failure to use sufficient digitalis, overexertion, etc., severe cardiac insufficiency occurred, as evidenced by a rapid and perpetually irregular pulse, dyspnea, hypostatis, etc., the urine at once contained greater or lesser traces of albumin, with casts. When compensation became restored the urine again became free. The attacks of decompensation became more frequent and became harder to control; finally, the heart lost its reserve and the patient died during an attack which began only about a week before he died. The autopsy revealed a great surprise. At the autopsy both kidneys showed an advanced nephritis of the contracting type. The cortex was only about ½ cm. thick, the markings were completely obscured and there were marked glomerular and interstitial changes.

Here, in other words, was a kidney so badly damaged that if we view the kidney simply as a filter we had reason to expect the most profound changes in the urine. On the contrary the urine was entirely normal and free from albumin, except when the circulation was at fault.

Incidentally, this case also proves that a contracted kidney is not always associated with a high arterial blood-pressure, as some would lead us to believe. I shall refer to the relation of contracted kidney to hypertension in a subsequent part of this paper.

The contention that albuminuria is the result or, at least, is modified by circulatory changes is paralleled by other observations. Every clinician knows that in frank valvular disorders of the heart albuminuria rarely occurs except during the stages of severe cardiac insufficiency. Furthermore, if it does occur during "compensation" it is invariably increased during the stage of insufficiency. This observation is especially significant in view of the well-known fact that in the chronically congested kidney the renal epithelium is unusually well preserved.

Furthermore, similar circumstances hold true in hypertension. When the patient, both clinically and objectively, is in the stage of good compensation the albumin remains quantitatively the same. When decompensation occurs the albumin increases. Moreover, and this is significant in both conditions, namely, valvular heart disease and hypertensive states, the improvement in the amount of albumin is directly influenced by treatment of the circulatory

failure alone. My own impression is that in these cases the amount of albumin is roughly proportionable to the diuresis.

The integrity of the kidney as a filter against albumin, therefore, depends in great measure upon fine adjustments of blood supply. Which are the forces in the dynamics of the circulation that disorganize this adjustment we can only surmise. Variations in arterial pressure alone cannot be entirely responsible, because sometimes an increase and sometimes a decrease may increase the quantity of albumin. Regularity or irregularity of heart action obviously plays no role. The only other factors that may be considered are three: blood velocity, volume flow and change in blood viscosity. Blood velocity is the rate with which a given volume of the blood flows passed a certain point. "By volume flow is meant the volume of blood passing through a vessel or organ in a definite time, independent of whether its velocity is great or small." (Wiggers.) Inasmuch as the volume varies with the size and weight of the organ, physiologists have calculated the minute volume flow in terms of 100 gm. of substance. By such a method it is found that the minute volume flow varies widely in different organs, being least in the lower extremity and greatest in the thyroid. Which of these three factors, variation in the blood velocity, the minute volume flow or blood viscosity, or a combination, is responsible for these variations in the albumin and kidney function it is at present impossible to say. My own guess is that all factors are responsible with the minute volume flow being by far the predominant one, for the reason that is more widely influenced by pathological conditions.

It is not generally appreciated, as it should be, that our present clinical methods of determining the function of the circulatory system furnishes us with only a limited and, above all, the least important information. We have excellent means of determining the rate, the rhythm, the pressure, the conduction impulses and the topography of the circulatory organs; but the most important information, namely, the actual work of the heart, we can only guess at. To determine the velocity and the minute volume, very complicated methods, requiring the facilities of a well-equipped physiological laboratory, are required.

Thus far we have only been discussing albuminuria as an evidence of disordered kidney function. We always regard albuminuria as the earliest and most constant symptom, probably because its clinical determination is the easiest. But albuminuria is not the only sign of disordered kidney function; functional tests also comprise the determinations of gravity and quantity, salt balance, the phenolsulphonephthalein tests, the quantitative examination of the blood for non-nitrogenous products, urea, creatinin, globulins and lipoids, etc. The correct interpretation of these tests has shown (1) that disordered kidney function is not a simple thing but covers a wide variety of pathological-physiological states. We are now able to

roughly group disordered kidney function into certain types, representing in our minds various clinical concepts. Unfortunately these clinical concepts have proved thus far to have no precise pathological foundation. In other words, we are still unable to predict the type of kidney or the amount of destruction of the different renal components we expect to find at autopsy, except to only a limited degree. The classification thus far is only a biological one. (2) Furthermore, these tests have shown that a disordered kidney function may be present even before albumin has appeared in the urine. It is therefore perfectly possible that had some of the above tests been applied to the patient I have mentioned, in whom an advanced chronic nephritis was found at autopsy, a disordered kidney function may have been discovered even during the periods when albumin was absent in his urine. It is not at all an unreasonable conjecture, therefore, that one of the above tests or one that may yet be discovered may prove to be a forerunner of a disordered kidney function even long before albumin is discovered in the urine; just as we know that the potential diabetic has an increase in blood sugar long before glycosuria appears.

Have we any demonstrable proof that a hypertension may occur without an anatomical nephritis? I have never seen one, but my experience is confessedly limited. However, the cases reported are sufficiently numerous to warrant the assertion that a patient may have hypertension, and may even die as the result of the hypertension, and yet have practically normal kidneys. These cases are comprised under the groups termed "essential" hypertension or "hyperpiesis." But I am as yet by no means convinced that the observations of those who report normal kidneys in hypertension are valid. My reasons for saying this are the following: (1) That in my experience a perfectly normal kidney in the middle-aged adult is almost never found. (2) That the interpretation of what constitutes a "nephritis" varies so widely even among pathologists. A nephritis does not necessarily constitute injury to the epithelium, but to the interstitial tissue and bloodvessels as well, and it is by no means uncommon to see kidneys, with seemingly intact epithelium, but with definite changes in the glomeruli and vessels, with or without slight round-celled infiltration or increase in the interstitial tissue. I would not mention this except that I know of one instance at least in which an experienced and well-known clinician reports a case of "hypertension without nephritis," although his accompanying illustration shows a well-marked round-celled infiltration of the interstitium. (3) I have performed autopsies on patients who had hypertension during life, in whom I found kidneys in every way normal, except that they showed slight or moderate degrees of round-celled infiltration in scattered areas of the cortex, with occasional hyaline change in the glomeruli. Now, as I have already intimated, there is nothing in pathology more apparent than the remarkable

lack of relationship between functional tests of disordered kidney function and the variety of kidney that we find at autopsy. Indeed, it is hazardous to predict the type of kidney, which the pathologist will find at autopsy from clinical findings alone, and that is why a classification of chronic nephritis on the basis of anatomical types has proved a failure. This is not surprising when we consider that even a classification of nephritis on an anatomical basis is attended by almost insurmountable difficulties. Witness, for instance, the bewildering confusion in classifications in current text-books on pathology. We find the "small red kidney," the "large and small white kidney," "parenchymatous nephritis," "glomerulonephritis," "interstitial nephritis," "tubular nephritis," "diffuse nephritis," "granular kidneys," "indurative nephritis," the " arteriosclerotic kidney," etc., and we are given to understand that each is a separate type, with a distinct and separate gross and microscopic lesion of its own.

Now upon what does the appearance of the disease of the kidney depend? It depends upon (1) the amount and character of alterations in the structure of the glomeruli; (2) upon the variety of degeneration and its extent in the tubular epithelium; (3) in the amount, character and situation of the replacement connective-tissue fibrosis; (4) upon the extent of the blood supply and the amount of sclerotic change in the bloodvessels; and lastly (5) upon the extent of the compensatory changes in the intact portions of the kidney parenchyma. We may therefore expect all kinds of appearances, depending upon the extent, variety and situation of these changes. *Such changes as I have described are present in practically every subacute or chronic inflammation of the kidney, so that in the strictest sense of the word every subacute or chronic inflammation of the kidney is a diffuse one*, involving glomerulus, epithelium, interstitial tissue and bloodvessels *en masse*. In some, lesions of the glomeruli are predominant; in others, the degenerations of the epithelium; in others, the growth of new connective tissue; but one is not found without the other. The interstitium may show only a slight scattered cortical round-celled infiltration, but such changes are not present without some lesions of the glomeruli or epithelium. Obviously, therefore, a classification depending upon the predominance of the lesion in a certain component of the kidney structure is entirely arbitrary and is not justified by facts. A glomerular nephritis is therefore a parenchymatous nephritis and an interstitial nephritis as well, and *vice versa*.

Microscopically, there is a striking morphological uniformity of the lesions no matter what "type" the kidney may be. In other words the only differences between the "large white kidney," the "red granular kidney" and the "contracted kidney" are in the extent and degree and maturity of the lesions. Indeed, the similarity microscopically is so striking that one cannot escape the thought that all these various types have one and the same patho-

genesis, and that, according to well-established morphological criteria, they merely represent stages of a single process. These kidneys therefore represent a scale in which, roughly, the first stage is represented by scattered round-celled infiltration of the cortex, with associated slight glomerular changes and degenerations of the epithelium; the next stage is represented in the so-called "white kidney," in which the round-celled infiltration is far more extensive and the changes in the glomeruli and epithelium are more marked and diffuse; a more advanced stage is the "red and granular" kidney, in which much of the round-celled infiltrations has become frank scar tissue; the glomeruli have become fibrous and hyaline while some of the intact tubules show compensatory changes in the form of small gray granulation-like elevations, which appear prominently above the cortex, and the capillaries are congested. Finally, we find the small, contracted kidney, in which the lesions of the various components are so marked and the amount of connective tissue is so dense that the structure has been completely disorganized. This is the only type of chronic nephritis that may be considered an end-product, for it is hardly conceivable how such an intense degeneration could proceed further, and it is equally not conceivable how such a deformed and scarred kidney could have resulted without having passed through such changes as I have described. The distinctions therefore that have been made between "primary" and "secondary" contracted kidney I hold, therefore, to be entirely unwarranted. These gradations are entirely analogous to the method of production of any interstitial change in any organ of the body, as in the liver, the uterus and ovary for instance, or that witnessed in the conversion of granulation tissue into scar tissue.

Therefore, with the exception of the contracted kidney, each of these types of kidney lesion, which I repeat is only exceptionally pure and nearly always mixed, represents a phase of a single progressive pathological process rather than a definite end-product. The type of kidney we shall find depends entirely upon the period in which the decompensation is no longer responsive to treatment. Each has potentialities, provided the patient lives long enough, to pass into a more progressive stage. Such a lesion, therefore, should not be regarded as the sole cause of death, but only as a greater or lesser contributing factor and as an incident in the pathogenesis of a chronic inflammation of the kidney. The primary cause of death may be conceived as a functional rather than an anatomical one.

I am not prepared to say that all chronic nephritides pass through all the stages that I have described. The effect of a toxin may be so profound, *e. g.*, scarlet fever, that even the earliest kidney change may be represented by a morphologically advanced glomerulonephritis, but in the vast majority of lesions associated with hypertension states the lesion, I believe, progresses in the manner I have described.

I believe, therefore, that the lesions represented under the term "Bright's disease" are not primary in the vast majority of instances and are not the direct cause of hypertension but represent the response to a continuous circulatory vasoconstricting influence or to the substance that brings about this influence.

My reasons for believing that certain forms of chronic nephritis are secondary to a persistent hypertension or of the causes of the hypertension are based upon the following propositions: (1) We have seen that clinically cases of hypertension vary from those which have no evidence of disordered kidney function (essential hypertension) to those in which evidences of disordered kidney function are profound (Bright's disease); (2) observation has shown that cases of essential hypertension, unless checked, sooner or later reveal evidence of disordered kidney function and that this progressively increases until the well-recognized clinical picture of Bright's disease is manifest; (3) pathologically, cases of hypertension vary from those which reveal none or slight lesions of the kidney at autopsy to those that show the full-fledged lesions of Bright's disease (contracted kidney); (4) from a morphological viewpoint these lesions, as I have tried to show, reveal a continuous and progressive series, beginning with those kidneys which reveal but slight fibroblastic and glomerular lesions in the cortex to the senescent contracted kidney; (5) the fact that the signs of nephritis may be cured or arrested in early cases by means that restore the hypertension to normal. This would obviously not be possible if we dealt with a primary progressive anatomical lesion.

These propositions, it seems to me, furnish sufficient circumstantial evidence to warrant the deduction that chronic nephritis is a secondary consequence and not a primary cause of hypertension. We are obviously not in the position to watch the transformation of the normal kidney of a case of essential hypertension into the progressive stages of the kidney of Bright's disease; until we can, such reasoning as I have offered must, it seems to me, guide us in obtaining this deduction.

There are, moreover, certain negative evidences that warrant the conclusion that the kidney lesion is not primary: (1) If a primary nephritis were the cause of a hypertension we should expect that the degree of hypertension would be proportionate to the degree of damage to the kidney. This, however, is by no means the case. (2) All experimental attempts to bring about a persistent hypertension by direct injury to the kidney or by removing large portions of the kidney parenchyma have proved futile. (3) Extensive destruction of the kidney by disease, *e. g.*, chronic infections, amyloid disease, subacute bacterial endocarditis, etc., which cause lesions comparable in their morphology to those of Bright's disease, does not result in hypertension. (4) Renal extracts have thus far failed to exert a continuous pressor influence.

The conception of many forms of chronic nephritis as being

due to increased blood-pressure makes me believe that perhaps after all those who have regarded chronic nephritis as a primary vascular disease, *e. g.*, Jores, are probably right. Certainly, no one can deny that lesions of the glomeruli are the most predominant and constant lesions in all stages and varieties of chronic nephritis. If such a conception is granted, arteriosclerosis and chronic nephritis may be considered as having one and the same pathogenesis, the lesion in each being modified by the nature of the organ. This conception requires much clinical, postmortem and even experimental investigation to confirm it. At all events the data thus far at our command seems to make this conclusion extremely probable, and I submit it for consideration.

Having eliminated the vast majority of kidneys associated with hypertension from the category of primary nephritides, what shall we say of those cases of disordered kidney function associated with normal blood-pressure? We shall eliminate at once amyloid kidneys, the kidneys of subacute bacterial endocarditis and the kidneys of acute mercurial poisoning, because this association has been established many times. There still remains a considerable number of cases, the exact nature of which has puzzled me for a long time. These patients consistently pass albumin, show nitrogen retention, have edema, dyspnea, etc., and yet the blood-pressure remains normal. Some undoubtedly belong to the group which Epstein calls "parenchymatous nephritis," the pathology of which is still, according to Epstein, entirely obscure. I am entirely in the dark as to the nature of the pathology of others, and I await an autopsy with intense interest.

The subject of the relation of hypertension to chronic nephritis, or, better said, disordered kidney function, is therefore rich with problems. My attempt to correlate the clinical and anatomical sides, inadequate as it is, will, I trust, serve to show from what aspects some of these problems need be studied, the solution of which may be of vast consequences not only to the understanding of these conditions but of failures of the circulatory system.

Etiology of Hypertension. The cause of hypertension has thus far not been satisfactorily explained. In text-books and medical writings most emphasis is placed on chronic nephritis and arteriosclerosis as the main "causes" of hypertension. I think I have shown, however, that the causative relation of chronic nephritis to hypertension is an extremely speculative one, with the strong probability, that it bears only a slight if any relation, and that the clinical findings expressive of a chronic nephritis in our mind represent rather a state of disordered kidney function than an inflammation of the kidney in the anatomical sense. Whatever changes we therefore see in the kidney at postmortem represent injury due to hypertension itself or of the toxin or toxins that cause the hypertension.

The evidence in favor of arteriosclerosis being a secondary con-

dition, due to hypertension and not the cause, is exceedingly strong and to my mind convincing.

The conception of the diseases associated with hypertension as due to "wear and tear" makes an unusual appeal. Such diseases almost always appear and progressively increase in frequency after the middle period of life, and, indeed, as Osler says, "To a majority of men death comes primarily or secondary through this portal;" apoplexy, uremia, cardiac failure and coronary disease account for the majority of deaths past middle life.

To describe a disease as due to "wear and tear" is hardly satisfactory, because such a cause is much too vague and remote. Is it possible to specify the conditions under which "wear and tear" are most likely to occur; are we able to state what elements comprised under the term "wear and tear" bring about these degenerative processes? In other words, why does not hypertension with its associated conditions affect all of us after we have reached the middle period of life?

I here beg leave to submit some observations that I believe bring us somewhat nearer to the solution. I have found that the greatest proportion of patients afflicted with hypertension conform to a certain type, which may be described as both physical and psychic. The patients are overweight and sometimes even obese. The neck is short, the muscles are soft, their bodily movements are sluggish, their carriage and walk are ungraceful and they lack the spring and *elan* of the former athlete. Psychically, these people are tense; they pursue their vocation with tremendous seriousness and worry over trivialities. In consequence they are irritable. Phlegm and hypertension are, in my experience, antagonistic. Furthermore, these individuals have narrow intellectual horizons. Their interest in anything outside of their business is desultory. They have no hobbies. In their leisure hours they play cards, sit in the theater, read the newspapers or rehearse the business activities of the day. Their sleep is not restful and they "do not believe" in vacations. Who cannot recognize in this picture the individual that has been facetiously termed the T. B. M., or "tired business man," whose tastes have activated a large portion of the so-called modern drama? He eats well, drinks alcohol to obtain the stimulation that his mental faculties do not afford, and his most violent daily exercise is his walk to and from the conveyance that takes him to his business. As a rule these people are "successful," and they may be said to die of "success." His most conspicuous mental incapacity is his inability to play. He is no longer a child. I take it that most of us have something of the child within us. Age is not always a matter of years. The greatest tragedy is when the spirit of the child goes early, as so often happens when it is blighted by the premature struggle for existence or the gloom of a depressing environment. Others keep it to a ripe, green age; others, like Peter Pan, never grow up. To be a child is to be able to make believe, to have fancy

and imagination, to be able to take things as they are and not as they think they should be, to live in the present and not in the past, to play lightly with the future, to hear with equanimity the stresses and strains of modern existence, to have ideals, to find some interest in everything, and, above all, to have a sense of humor. What sense of humor is so perfect as that of a child? The child lives in an unreal world and in one of his own making, but who shall say that it is not the only world worth living in? Pity upon him who has no illusions. All these things remain in him who keeps his childhood despite the threat of advancing years. He may be restrained by convention or mellowed by a ripening wisdom, but they are there, coloring his conduct and his philosophy. The child, as he grows older, becomes a sport and always remains a sport. This applies not only to his participation and interest in athletics, but especially in his years of discretion, to his conduct of affairs; he is willing to take chances and accepts the "bludgeonings of chance" calmly and with grace.[2]

The individual with hypertension, you will find, on the other hand, lacks these attributes wholly or in a large measure, and is mentally and physically prematurely old. To my mind it is the psychical as much as the physical that brings on premature old age. A well-balanced life requires play as well as work, an alkali, if you may so put it, to neutralize the corroding acid of the "fret and fever" in our lives. When a famous clinician said that "we are as old as our arteries," he spoke truer than perhaps he knew.

These influences apply to the rich as well as to the poor, and although I have confined myself largely to the aspects of the problem in man because it is most common in the male sex, women are subject to precisely the same influences. They apply to the laborer as well as to the brain worker, although, for obvious reasons, hypertensive states are more common in the latter—to the professional man as well as to the man of business. I have often thought that the reason why deaths from hypertensive states are less common in those who pursue the arts, literature, music, sculpture, painting, etc., is because in these vocations the element of play is largely mixed.

I think most of us have seen families in which hypertensive states seem almost hereditary. This seems to me readily understandable when one considers that the complex I have described is more directly traceable to environment than to heredity. This is another instance which to my mind indicates that acquired characters are not transmitted in the Weissmanian sense.

Why psychical and physical influences, such as I have mentioned, should bring about a continuous vasoconstriction of the arteries, with its secondary consequences, I cannot, of course, explain. It cannot be mechanically explained by the overweight alone, because

[2] Roosevelt is the representative of this type. In literature, Barrie, Stevenson, Riley, Field and Mark Twain expressed the spirit of the child in their writings as no one else ever did.

we know that stoutness alone does not bring hypertension. The theory of Cannon, which supposes that under the stimulus of mental excitement the adrenalin content of the blood is increased, with occasional glycosurias, is very alluring for purposes of explanation. Unfortunately, the work of Cannon has not been confirmed. Furthermore, it has been definitely shown that small increases in the blood adrenalin do not cause an increase in tension, but the reverse. In this connection I cannot resist the temptation to add that in my experience many patients with diabetes have the precise mental character that I have described above and that hypertension and certain forms of diabetes possess many parallel clinical features. Why the same cause should lead to diabetes in the one and to hypertension in the other I am at a loss to explain.[3]

Obviously, I am not trying to account for all cases of so-called essential hypertension by this etiology. Once in a while, if rarely, we do meet people with hypertension who do not conform to the complex I have mentioned. I recall patients, for instance, whose malady seemed to be directly traceable to syphilis, to lead and to scarlatina. Even in such instances may it not be possible that the poison is primarily vasoconstricting and that the arterial and kidney lesion is a secondary phenomenon?

There may be other vasoconstricting influences than that which I have described, but, at all events, I hold that the vast majority of patients with hypertension will be found to conform to this type.

Conclusions. 1. A persistent hypertension represents, in the strictest sense, a decompensation of the circulation. Moreover, the subjective and objective phenomena of decompensation represent a progressive process, and every persistent hypertension, unless complicating factors are introduced, will eventually result in the graver evidences of decompensation represented by the clinical picture of cardiac insufficiency.

2. The signs of decompensation may be both subjective and objective and there is only an approximate parallelism between the two. Subjective improvement or deterioration does not always correspond to objective improvement or deterioration and *vice versa*.

3. Many early cases of essential hypertension, in which both systolic and diastolic pressure are not too high, are as far as present observations lead one to believe, entirely curable.

4. The conventional classification of hypertension into essential arteriosclerotic and nephritic is not justifiable on etiological grounds. Such a classification is merely clinical and teleological. On such a basis, the classification should include the cerebral, cardiac (coronary) and aortitic types in addition to the above.

[3] These same psychic influences may serve to explain why hypertensive states are so very commonly the causes of death in physicians, as the annual reports in the Journal of the American Medical Association eloquently testify. Owing to the strain of their vocation, physicians are extremely apt to fall into the state of mind I have described and for the same reason take little physical exercise.

5. The vast majority of disorders associated with persistent hypertension begin as "essential" hypertensions. If untreated such essential hypertensions lead to the clinical concepts of arteriosclerotic, nephritic and other hypertensions.

6. All available evidence at present under our command seems to show that arteriosclerosis (with the possible exception of the "decrescent" form of Clifford Allbutt) is the result of the hypertension itself or (less likely) of the cause that brought about the hypertension.

7. Albuminuria is not necessarily the result of injury (even profound) of the kidney parenchyma. Badly diseased kidneys may be present without albuminuria.

8. The albuminurias associated with cardiovascular disorders (valvular heart disease, hypertension, etc.), are more the result of static circulatory changes within the kidney than to direct injury of the kidney parenchyma. Which forces in the dynamics of the circulation bring this about we can only surmise.

9. Functional tests of kidney function have thus far only furnished us with a biological classification. Both clinical signs and functional tests do not permit us, except in a limited degree, to diagnose the anatomical "type" of nephritis that will be found at autopsy.

10. A hypertension may occur with normal kidneys or kidneys practically normal.

11. The confusing nomenclature and classification of "types" of chronic nephritis is due to the fact that the attempt has been made to define each "type" as the result of a specialized form of injury. Evidence is adduced to show that the majority of these various "types" are the stages of one and the same pathogenesis. Such types are therefore not end-results, with the exception of the "contracted" kidney. The "type" of kidney we shall find at autopsy depends upon that period in the pathogenesis of his malady in which the patient succumbs.

12. Evidence is adduced to indicate that in many instances at least, the pathological changes in the kidney of Bright's disease are the results her than the cause of hypertension. Such a conception would render it very probable that the hypothesis of the primary vascular origin of the lesions in the kidney in Bright's disease is correct. Arteriosclerosis and Bright's disease have therefore the same pathogenesis, the lesion in each being modified by the nature of the organ.

13. The direct etiology of hypertension is unknown. However, a type of person is described, conforming to certain physical and psychic complexes, in whom hypertension is very likely to occur. This type is the antithesis of the child, both in mind and spirit. A knowledge of this type may prove of value in prophylaxis.

MENINGO-ENCEPHALITIS AS THE ONLY MANIFESTATION OF MUMPS: REPORT OF THREE CASES.

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During the past winter, at Camp Lee, we have been afforded a rare opportunity of studying mumps in adults. Nine cases of cerebral complications in frank cases of mumps have been encountered and have been made the subject of a special report by Lieut. R. L. Haden,[1] who has had the supervision of the Contagious Disease Service.

These cases were characterized by the occurrence, during an attack of mumps, of increased temperature, headache, vomiting and frequently evidence of cerebral disturbance, as stupor, delirium, etc. Lumbar puncture usually showed a moderate pleocytosis of a mononuclear type, and the physical signs of a mild meningitis were usually present. Haden shows that in some cases evidence of any meningitis is lacking and in most others the accompanying encephalitis is the predominating factor, and concludes that the cerebral complication of mumps is mainly an encephalitis rather than a meningitis.

The object of this paper is to put on record the history of three cases which exactly parallel the frank cerebral complication of mumps as observed at this hospital, except for the absence of involvement of the salivary glands or testes.

Metastatic lesions in mumps are well known, testifying to the general nature of the infection. Orchitis, mastitis, pancreatitis, arthritis, encephalitis and meningitis are at times met with. Furthermore, during an epidemic at least one of these complicating conditions—orchitis—is at times recognized in the absence of any involvement of the salivary glands. There is therefore no reason to doubt that one or more of the other unusual manifestations of mumps infection may occur without salivary gland involvement.

The three cases reported below are regarded as instances of mumps meningo-encephalitis, in spite of the absence of inflammation of the salivary glands, for the following reasons:

1. They occurred in the presence of a mumps epidemic.

2. Two of the patients had never had mumps, while the third (Case II) had been told by his father that he had had mumps, but could not remember it himself.

3. They all presented mild symptoms of meningo-encephalitis, which were entirely relieved or much ameliorated by spinal puncture.

4. In two of the three cases (Cases I and III) there was recovered from the spinal fluid a Gram-positive diplococcus. This was found

[1] Arch. Int. Med., 1919, xxiii, 737.

in direct smear and grown in pure culture in both cases. In Case III it was found in smear three times and recovered in culture twice.

That mumps is due to an organism of this description has long been believed, and further evidence to this effect is adduced by Lieut. Haden from evidence accumulated at Camp Lee.

5. The spinal fluid in each case presented a moderate pleocytosis, characterized by a predominance of mononuclear cells. The conditions with which we are familiar, which show this picture, are (*a*) syphilis, (*b*) sometimes tuberculous meningitis, (*c*) encephalitis lethargica and (*d*) mumps.

(*a*) As to syphilis, two of the patients were negative serologically and the third (Case III) while having a positive Wassermann, repeatedly showed the presence of a Gram-positive coccus in the spinal fluid. Thus two of the three patients were certainly not syphilitic and the third certainly had some infection besides syphilis.

(*b*) Tuberculous meningitis is ruled out in all cases by the clinical course.

(*c*) The same may be said of encephalitis lethargica, there being no cranial nerve involvement and no palsies of any kind. There was also lacking the increase of tendon jerks which was almost uniformly present in the cases of this disease which we have observed.

Unless we presume to hypothecate some unknown type of infection, we are forced by exclusion to consider the three following cases as meningo-encephalitis due to mumps.

Case I.—D. W. M., Sgt., Q. M. C. (4630924), admitted to hospital March 24, 1919; aged twenty-one years, white; seven months service; a native of Washington, D. C. His premilitary occupation had been that of a clerk.

The family history was negative, his parents, a brother and two sisters being alive and well.

Previous Personal History. In childhood he had had measles, whooping-cough and scarlet fever, which was followed by mastoiditis. At thirteen he had had grip. He stated that he had never had mumps. He denied venereal disease.

History of Present Disease. For a week before admission to the hospital he had had a dull headache and felt dizzy at times, but had remained on duty. There had been no disturbance of vision and no complaint of digestion or respiratory symptoms. He stated that he had had fever for one day and the headache had become more severe.

On admission, 8.30 P.M., his temperature was 99.8°, pulse, 78; respiration, 18. Physical examination was essentially negative. The next morning the temperature was 101.4°, with a pulse of 80. The pupils were equal and reacted to light. Extra-ocular movements were normal. The tongue was protruded in the median line and there was no muscular weakness of the face or elsewhere. Forced

[1] Am. Jour. Med. Sc., 1919, clviii, 698.

flexion of the neck was a little painful and induced drawing up of the knees. The tendon jerks—biceps, patella, Achilles—were symmetrical and normal, as were the abdominal and cremasteric reflexes. There was no Kernig and no Babinski. The chest and abdomen were negative.

The throat was slightly injected. There was no eruption on the skin. There were 9000 leukocytes, the differential showing 69 per cent. polymorphonuclears; 21 per cent. lymphocytes; 9 per cent. large mononuclears and 1 per cent. transitionals. The urine was 1.030 specific gravity, and showed a faint trace of albumin, a few leukocytes and amorphous urates. Blood culture was negative.

Lumbar puncture showed the spinal fluid to be under moderate tension and 25 c.c. were removed. The fluid was clear and contained 360 cells per c.mm., of which 99 per cent. were mononuclears. The test for globulin was reported negative and the Wassermann was negative. In the smear were found Gram-positive diplococci, which were grown in pure culture.

The patient was much more comfortable after the spinal puncture. His temperature was 99° the next day and remained normal there after. He was discharged to duty April 8, 1919.

Case II.—G. H. H., Jr., Sgt., Medical Corps (1845685), admitted to hospital May 11, 1919; twenty-five years of age, white; two years and two months service; a native of Kentucky. Before enlistment was a railway messenger.

Family History. Father living and well. Mother died of typhoid fever.

Previous Personal History. Inflammatory rheumatism at the age of nine. Patient stated that his father told him he had had the mumps at the age of nine, but that he did not recall having had the disease. He had had an appendectomy and an operation for hemorrhoids one year ago. In 1917, before entering the service, he had had a "scratch" on his penis, and although he had never had any symptoms of syphilis and never had a Wassermann done, he had taken several doses of salvarsan "to be on the safe side."

Present History. The day before admission he began to feel very tired and complained of pain in the head and back. The following day he felt much worse and complained of pain in all his joints and stiff neck.

On admission his temperature was 100.8°; pulse, 76; respiration, 18; and he was very uncomfortable. The pupils and extra-ocular muscles showed no abnormality. The neck was stiff. The tendon jerks and skin reflexes were normal and equal. There was a definite Kernig's sign on both sides, which was more marked later. There were no palsies. The chest and abdomen were negative. The throat was somewhat reddened. The skin showed no eruption and the glandular system was negative.

There were 16,400 leukocytes, of which 78 per cent. were poly-

morphonuclears, 15 per cent. lymphocytes and 7 per cent. large mononuclears. The urine was 1.016 in specific gravity and contained no albumin or casts. Blood culture was sterile. Wassermann was negative.

Lumbar puncture showed the spinal fluid to be under considerable pressure and slightly turbid. It contained 703 cells per c.mm., of which 90 per cent. were mononuclears and 10 per cent. polymorphonuclears. Globulin was present. Smear and culture showed no organisms.

Wassermann was negative. The patient was given 30 c.c. of antimeningococcic serum at the time of the first puncture. He improved rapidly, his temperature never exceeding 99° after the second day and remaining normal after the fifth. The stiff neck and Kernig's sign persisted for about ten days. A second spinal puncture was done on May 14. The fluid this time showed 530 cells, of which 80 per cent. were small mononuclears, 18 per cent. large mononuclears and 2 per cent. polymorphonuclears. Globulin was increased. Sugar was present. Smear and culture disclosed no organisms.

This patient's recovery and convalescence were less prompt than in the case of the first patient, but he was discharged to duty in good condition on June 5, 1919. He received no antiluetic treatment.

CASE III.—J. M., Sgt. 1/c. Q. M. C. (1843176), aged twenty-nine years; one year and nine months' service; a native of New York, was admitted to the hospital, April 19, 1919.

Family History. Father, mother and four sisters living and well.

Previous Medical History. Had gonorrhea three times prior to entering the service. About four months previous to admission had a venereal sore. A Wassermann was found to be ++ and he was given nine injections of salvarsan and eight of mercury, the treatment lasting up until shortly before he came into the hospital. In January, 1919, he was kicked in the back by a mule, but this caused him practically no symptoms.

History of Present Disease. About a week before admission to the hospital he began to suffer from a boring pain in the small of the back, occurring in the early morning hours. After entering the hospital he complained also of headache. There were no other symptoms. His temperature was normal and has remained so except for an occasional rise to 99° and once to 100°. The pulse and respiration were normal. No local pathology was found to explain the painful back. The Wassermann was negative and no focal infection could be found. The urine showed a faint trace of albumin and a few leukocytes. There were 4,000,000 erythrocytes, 7200 leukocytes, of which 59 per cent. were polymorphonuclears, 18 per cent. small mononuclears, 19 per cent. large mononuclears, 2 per cent. eosinophiles and 2 per cent. basophiles.

On April 29, 1919, examination showed pupils equal and active. Extra-ocular movements normal, other cranial nerves negative. Slight stiffness of neck. Some resistance on extending leg on flexed thigh, but no pain. Deep reflexes normal. Abdominal not obtained. Babinski negative.

A lumbar puncture showed no increase of pressure, but the fluid was slightly turbid. It contained 2500 cells, all lymphocytes, globulin present, sugar negative, Wassermann ++ (0.5 and 1 c.c.). On smear and culture was found a small Gram-positive diplococcus. The data obtained on repeated punctures is shown in the table. The headache and backache were relieved shortly, but after about a month the pain in the back recurred. He has received no antileutic treatment while in the hospital, in spite of which the Wassermann steadily declined in intensity and the number of cells markedly decreased. It seems probable that the presence of a secondary infection actuated a latent syphilitic lesion, and with the subsidence of the former it is planned to begin active treatment. (See Table.)

SPINAL FLUID FINDINGS IN CASE III.

	April 29.	May 5.	May 14.	May 26.	June 5.
Cell count per c.mm.	2500	1200	390	140	300
Mononuclears, per cent.	100	100	98	100	
Globulin	+	++	+	+	±
Sugar	0	0			
Organisms on smear	+	+	+	−	−
Organisms on culture	+	+	−	−	−
Wassermann, 0.5 c.c.	++	++	+	+	−
Wassermann, 1.0 c.c.	++	++	++	++	+

MYXOMA OF THE HEART SIMULATING BRONCHOPNEUMONIA.

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(From the Base Hospital Laboratory, Camp Jackson, S. C.)

The presence of primary neoplasms of the heart usually presents during life such obscure symptoms that little has been written upon the subject. Most text-books pass the subject over in a few words, which, summed up, amount to saying that it is impossible to make the diagnosis or that it is only made by exclusion. In view of the fact that modern surgery makes intrathoracic surgery a comparatively safe procedure, I feel it is essential to report all such cases in detail in the hope that eventually a symptom-complex for cardiac tumors may be worked out.

Private J. S., aged twenty-nine years, white, was admitted to the hospital October 8, 1918, with the diagnosis of pneumonia. The family history was negative. As a child he had diphtheria, scarlet

fever and pertussis, and three years ago an appendectomy followed by a laparotomy for intestinal obstruction. Two weeks before admission to the hospital the patient was observed by two comrades, who said he fainted twice at drill and on other occasions had to fall out of ranks when double-timing on account of shortness of breath and palpitation of the heart. The patient stated his present trouble began two weeks ago with a cold and a cough. The day before admission to the hospital, after a wrestling match, he began coughing a great deal and raising a considerable amount of blood, which became rusty on the following day. There was some abdominal pain and a burning sensation in the epigastrium, which gradually became more severe. No chill or pain in the chest. No nausea or vomiting. From that time breathing gradually became more difficult.

On admission the temperature was 99.4°, the pulse 146 and the respiration 52. Three hours after admission physical examination showed a well-built man with an anxious expression to the face. He was moderately cyanosed, was breathing rapidly and had a moderately accelerated pulse, but regular and of fair volume. The size and position of the heart were normal, the P. M. I. was in the V. i. c. s. inside the nipple line. No murmurs were heard. The muscular quality of the first sound at the apex was impaired and diastole shortened. The white blood count showed 17,800, of which 17 per cent. were small mononuclears, 7 per cent. large mononuclears and 76 per cent. polymorphonuclear neutrophiles.

There was impaired resonance with bronchovesicular breathing and slightly increased voice sounds over the right front down to the third rib. Similar but less distinct signs over the left front were observed and numerous medium and fine rales over the entire chest were heard. The opinion at this time was:

I. Acute toxic myocarditis.

II. Bronchopneumonia.

Eight days later the cardiac and lung conditions were much improved; the color was good. The pulse was slower and the breathing was slower and easy. The lungs were practically clear and the temperature normal.

On October 22 the temperature was 99° A.M., 100° P.M.; the pulse was 82, regular and good volume. His mind was somewhat confused and he was excited. The pupils were unequal, the right being larger than the left; both reacted, however, to light and accommodation. There were a few crepitant rales at the left base.

On October 24 the patient's orientation was a little disturbed; he had some delusions and at times was morose and would not answer questions. The pupils were still unequal, the right not reacting to light and the left only slightly. The tongue protruded in the midline. The knee-jerks were equal. There was a right ankle-clonus. The lungs were clear on auscultation and percussion. The heart apex was in the fifth interspace inside the

nipple line. No murmurs were heard. The pulse was soft, regular and 84 per minute.

The spinal fluid on this date showed three white blood cells and gave a negative Wassermann reaction. A white cell count showed 10,700, of which 17 per cent. were small mononuclears and 83 per cent. polymorphonuclears. The urine was negative except for mucous shreds and calcium oxalate crystals. The temperature, pulse and respiration were normal.

October 31, patient was seen by a psychiatrist and a tentative diagnosis of dementia precox made.

November 18 the patient tried to drink creolin, but apparently did not get more than a swallow. Prompt treatment was followed on the next day by apparently his normal condition.

November 20 a few rales were observed at the base of the right lung. The heart was normal to auscultation and percussion.

November 27 the patient was again examined by a psychiatrist, who made the following statement: "He had a severe attack of pneumonia, beginning about October 8, 1918, which was followed by the manifestations of his present trouble. There have been no injuries which have a bearing on his present trouble. He is well-nourished. There are no paralyses, tremors or tics. There is no disturbance of gait or station. The K. K. are increased but equal. The abdominals are present and there is no Babinski. The pupils are widely dilated, equal, regular and have a prompt but rather narrow reaction; there is neither nystagmus nor diplopia. There is no demonstrable disturbance of cutaneous sensation.

During the convalescent period from pneumonia this man developed a mild depression, auditory and visual hallucinations and ideas of persecution and poisoning, all of which have persisted up to the present time and have been slightly on the increase. His reaction to these has been one of depression and apprehensiveness, and on one occasion he attempted suicide by taking a mouthful of creolin. His memory and orientation are quite disturbed, and he has no insight. Retardation and blocking of thought are much in evidence. Diagnosis: Dementia precox."

December 28 the temperature was 97°, the pulse 120 and the respiration 28. Over the left upper chest in front, just outside the nipple line, a patch of high-pitched breathing was observed; lower down just below the apex of the heart a second patch of near-bronchial breathing, and over the right upper chest numerous large moist rales were observed.

December 29, exitus.

Temperature	98.2	
Pulse	118	
Respiration	40	
White blood cells	48,400	
Polymorphonuclears	95	per cent.
Small mononuclears	3	"
Large mononuclears	2	"

AUTOPSY. The patient was a well-built and fairly well-nourished man, 5 feet 10 inches in length. There were a few fragile adhesions in both pleural cavities, but no fluid. The pericardial sac contained 80 c.c. of clear, yellowish fluid. The peritoneal cavity was free from fluid or evidence of recent inflammation. The lungs were voluminous and firm, the right more so than the left, but both gave a slight crepitus everywhere on palpation. The cut surface was like liver tissue in consistency, and was dripping wet with fluid. The tissues were everywhere air-containing and blocks floated in the fixing fluid. The other organs showed the usual picture produced by back pressure. The brain and cord were not examined. The heart was enlarged, weighing 510 grams. The left auricle was filled by a tumor mass which was implanted by a broad base on the auricular wall. It was made irregular by polypoid-like growths, apparently growing in the line of least resistance, bulging the fossa ovalis into the right pulmonary vein, another into the mitral orifice and so completely filling the cavity that it was difficult to pass a small flexible probe between the tumor and auricular wall into the left ventricle. Thus a very effective resistance to the flow of blood in either direction was formed, owing to the pressure of the tumor against the distended elastic auricular heart muscle.

FIG. 1.—Photomicrograph. Showing spindle- and stellate-shaped cells. × 430.

The tumor was composed of two distinct portions, but attached to each other. The upper portion, which was quite firm but elastic, was attached to the heart wall, while the lower portion, which was comparatively soft and gelatinous, was an outgrowth from the hard portion and hung free from the heart wall. The harder portion

came down to the level of the coronary artery and the smaller and softer portion extended below the coronary artery, hanging as a free plug between the mitral valves. It measured 9.5 cm. in length and 8.5 cm. in its widest diameter. Complete closure of the mitral valves was impossible, and there was no reason why a regurgitant murmur should not have been produced except in so far as the ball-and-socket action of the tumor served that purpose,

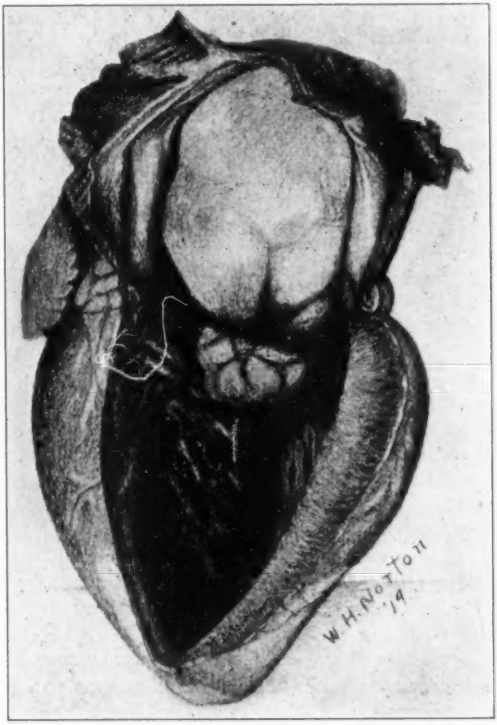

FIG. 2.—Showing the shape and position of the tumor, with reference to the valves. ×¼.

together with the distended auricular wall pressing against the tumor. The left ventricular wall was normal in thickness and the right was hypertrophied. The valves were normal. The tumor was covered by endocardium. On cross-section the tumor showed a preponderance of white, fibrous-looking tissue in the larger portion, but scattered here and there through it and preponderating in the smaller portion were rather clear dark-looking areas having a distinct jelly-like appearance. These latter areas

were quite definitely better supplied by bloodvessels than the white, fibrous-looking tissue and were definitely elastic.

Microscopic examination of sections in this case showed edema of the lungs and passive congestion of the liver, spleen, pancreas, kidneys and adrenals. The heart section showed the pericardium, myocardium and endocardium normal, with the exception that the endocardium over the tumor was thickened and the tumor growth immediately adjoining the muscle shows remnants of muscle bundles in among the fibrous and connective tissue. Deeper into the tumor there was a decrease in the number of cells having nuclei, although this varied, and there was a preponderance of granular intercellular substance taking a blue stain-like mucin. The cells in these areas were fusiform and stellate, one finding two, three and occasionally four protoplasmic processes to one nucleus. These areas were well supplied by bloodvessels filled with blood, which had a definite endothelium and elastic tissue in the walls. The elastic tissue was best shown by Mallory's elastic tissue stain. There were two other types of cells found: a few small round cells, with very little protoplasm and larger cells, with a slightly irregular nucleus and a nucleolus showing scarcely any protoplasm. In some places the cells were thick, in others scattered, forming strands in among the blue-stained portion. The round and oval nuclei were stained an intensive blue. These cellular elements were spread out over the entire section—in some places thick, in others thin. While the cellular areas were sometimes found in the rim portion they were most common in the central portion of the tumor. Between the cellular areas, but mostly around the periphery of the growth, one found eosin-staining tissue poor in nuclear elements and having definite wavy tendrils. In some portions considerable hemosiderin was found. There were a few areas in which small hemorrhages had occurred. The vessels were, for the most part, found in the areas with the greatest number of cells while the hemorrhagic areas were most often found in the rim portion. With the high power in those places where the cells lay closest together one found cells with long nuclei approaching the spindle cell in type and in between these cross-sections of cells which resembled round cells. Situated around the rim of the above-mentioned cell groups were star-shaped cells, with oval nuclei whose protoplasmic processes appeared to communicate with one another.

Here also were cells whose nuclei were definitely undergoing degeneration. These cells were probably degenerated myxomatous tissues which formerly were the above-mentioned spindle-shaped cells. Between these cells there was a fine-grained intercellular substance taking the blue stain with hematoxylin. Outside of these areas one found fibrous and connective tissue in which small hemorrhages were noted. Throughout the tumor elastic fibers could be seen. A few of the bloodvessels contained some fibrin.

The vessels were lined by a single layer of cells, and with an elastic tissue stain some of them showed a small amount of elastic tissue. They were, for the most part, filled with red blood cells.

While some might make a diagnosis in this case of fibromyxoma, I prefer to call it a true myxoma. There does not seem to me any more reason for calling a myxoma a fibromyxoma than there is for calling a carcinoma a fibrocarcinoma. Undoubtedly in this case there is considerable fibrous tissue present, but it is evidently replacing the degenerating myxomatous tissue. Thorel believes that myxomata are merely degenerating forms of organized thrombi. The chief arguments against this view are:

1. The presence of elastic tissue throughout the tumor.
2. Organized thrombi tend to contract and become smaller.
3. If they are organized thrombi and grow the oldest or densest scar tissue would be in the center of the tumor, which would be contrary to the usual procedure of organizing thrombi.
4. Why should 75 per cent. of all intracavitary tumors be localized in the left auricle when thrombi are equally as frequent in the ventricle as the auricle.

Myxomata form about 30 per cent. of all primary tumors of the heart if the reported cases can be relied upon as being correct. Unfortunately some of the cases reported are so brief that it is impossible in many cases to judge from the descriptions what was the nature of the tumor. Hektoen calls attention to the fact that the heart and hence its primary tumors are of mesoblastic origin. Hence it would necessitate a complete description before one could determine that a tumor was epiblastic or hypoblastic in origin.

Discussion. Link proposes to divide primary tumors of the heart into four groups for the study of their clinical symptomatology as follows:

Group I. Tumors developed in the auricles. The characteristics of these neoplasms is to produce a very marked stasis in the lesser as well as the greater circulation. During life it may have been impossible to explain this stasis, which did not depend upon any ordinary cause.

Group II. Comprises pedunculated tumors arising in the left auricle filling its cavity and sometimes penetrating through the mitral orifices into the left ventricle. These tumors produce symptoms of stenosis and insufficiency with disturbances of compensation. The signs here on auscultation are very variable and change with the position of the patient.

Group III. This group is composed of tumors having as their principal seat the right ventricle. The symptoms have been about the same as those of angina pectoris, with sudden death.

Group IV. In this group are placed tumors of the left ventricle and tumors of the valves where edema, dyspnea and undoubted

signs of aortic insufficiency were present. These patients die a sudden death without having offered any special symptoms during life.

Meroz in his paper proposes to group cardiac tumors for study according to their site:

1. Valvular tumors.
2. Intramuscular tumors.
3. Intracavitary tumors.
   (*a*) Sessile.
   (*b*) Pedunculated.

He summed up his observations by saying that primary tumors of the cardiac valves remain either silent and unsuspected or else produce phenomena of stenosis or insufficiency. Primary intramuscular tumors on examination reveal nothing or almost nothing which can explain the clinical manifestations. Sessile intracavitary tumors of the left heart can in no way be distinguished from organic cardiac affections. The pedunculated intracavitary growths are to be distinguished from organic valvular affections of the heart by producing an exceptional continued intense dyspnea, for which no satisfactory explanation can be given; by producing rather indistinct and particularly very variable signs of insufficiency or stenosis and lastly by the production of multiple emboli.

In the case herein reported the symptoms of stasis in the lesser as well as the greater circulation would cause one to place it in Link's Group I, with the exception that the physical signs and leukocyte count on admission would lead one to make a diagnosis of bronchopneumonia in spite of the fact that the temperature was never high and most of the time perfectly normal. Hence we cannot say with Link that during life it was impossible to explain this stasis. Link's Group II comprising pedunculated tumors arising in the left auricle filling its cavity and sometimes penetrating through the mitral orifice fits the location of this case exactly. However, Link's Group II calls for symptoms and signs of stenosis and insufficiency with disturbances of compensation. The only symptoms corresponding to this classification were cyanosis, dyspnea and palpitation, while there were no signs of stenosis or insufficiency on auscultation. As regards Meroz's classification, this case would be placed in the group of pedunculated intracavitary tumors; however, there was no continued intense dyspnea, no signs of insufficiency or stenosis and at no time any indication of embolism—in fact, none of the distinguishing features as outlined by Meroz were present.

Bodenheimer says the symptomatology of cardiac tumors is still a vast field open to investigation, that the symptoms produced are not precise or well defined and that they depend upon the size of the tumor. If it occupies a position which interferes with the heart's action it will set up phenomena of stenosis or insufficiency and the diagnosis can be made only by exclusion.

Berthenson states that in cases in which the clinical picture of the disease is indistinct and presents deviations from the normal type which cannot be accounted for, multiple emboli may give rise to the idea of a cardiac tumor. Ely insists on the fact that primary tumors of the heart do not give rise to much if any disturbance nor to any characteristic symptoms. Fränkel maintains that a pericardiac hemorrhagic fluid collection recurring quickly after puncture when the patient is not in receipt of a traumatism, and has neither tuberculosis nor scurvy, almost certainly indicates the presence of a cardiac neoplasm. Victor Petit emphasizes the fact that the symptoms are intermittent, one may hear a murmur, but its intensity and location may vary or it may appear then disappear altogether. In addition to the above facts we have to consider the fact that some cardiac tumors are never recognized or give no indication of their presence either on account of their size or their location. Such cases either result in sudden death without previous symptoms and are recognized at autopsy or are incidentally found at autopsy during examination for some other affection.

By taking a number of cases in which the histories are adequate and the patients gave symptoms and making a composite picture there is at once noticed an overlapping of certain diagnostic points. These points are dyspnea, general weakness, anemia, depressed mental condition, palpitations of the heart, a pulse of low tension and variability of all signs and symptoms. In many of these cases there may have been some overshadowing symptom, such as intense precordial pain, intense distress, with no relief except when sitting on the edge of the bed with the feet hanging down or signs of stenosis or insufficiency. None of these cases presented all of the symptoms at one time and all of them varied from day to day and week to week; this applies not only to the minor symptoms but to the major symptoms as well. It would appear then as if it were impossible to make the diagnosis of heart tumor from one examination that it must be made from a composite picture perhaps made up from several days' or weeks' observation. I agree with Victor Petit that the intermittent character of the symptoms should be emphasized most. Organic heart lesions like stenosis or insufficiency do not produce symptoms one day only to disappear on the next.

The variability of the symptoms must be dependent at least to some degree upon the position of the tumor, with reference to the blood flow; if the pedicle of the tumor is long it is easy to see how, as Petit suggests, the variability depends upon a torsion of the pedicle; in my case, however, the pedicle was so broad and thick that there was no possibility of torsion occurring. There was so much dilatation of the auricle from the tumor growth that the muscle must have been constantly giving away from necessity to accommodate the tumor and to allow the blood from the lungs to

pass through the auricle partially forced by the blood-pressure in the lesser circulation and partially by the dilatation occurring during diastole. As noted in the pathological examination, there was a polypoid-like growth developing into the lumen of the right pulmonary vein, introducing more resistance to the blood-flow from the right lung, hence the more marked signs on auscultation over the right chest.

If the intermittent character of the symptoms is in any way due to the accommodation of the anatomical structures to the size of the tumor then the nature of the tumor and its rapidity of growth would have an important bearing on the return of symptoms.

THE BACTERIOLOGY OF MUMPS: REPORT OF FINDINGS AT CAMP LEE.

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It seems surprising that so little is known about the virus of mumps. The disease is so common, so widely distributed and so prone to occur in epidemic form wherever numbers of people are collected together that one could expect to find numerous bacteriological reports of the disease in the literature. An unusual opportunity has been afforded in the army camps for a study of the disease. However, the mildness of its course and the fact that spontaneous recovery is the almost invariable outcome have largely removed the incentive for research work on its cause.

From time to time observers have isolated bacteria from the blood, the parotid secretion and the testis of patients suffering from mumps. The organisms recovered have been quite uniformly Gram-positive diplococci, which grow slowly in cultures, usually not appearing for forty-eight hours. Attempts to reproduce the disease with the cocci isolated have been for the most part fruitless. Herb[1] reports the recovery of a Gram-positive diplococcus from the heart's blood and tissues of a patient dying subsequent to an attack of mumps. This organism corresponded culturally with the cocci previously described by other investigators, and when injected into the parotid gland of a dog, caused a parotitis simulating mumps. The injection of cultures intraperitoneally also produced an orchitis.

More recently the view has been prevalent that the disease is caused by a filterable virus. This view is due largely to the failure of investigators to constantly reproduce the disease in animals with the organisms isolated. Wollstein[2] believes that the cocci which

[1] Jour. Am. Med. Assn., 1908, li.

[2] Jour. Exper. Med., October, 1918.

have been described are really all contaminations. She has injected cats with both the filtered parotid secretion and the blood of patients suffering from mumps, and considers that the results obtained justify the conclusion that the disease has been reproduced. However, the results are not striking, and there seems a reasonable doubt, from the description given, whether the condition produced by filtered secretion on injection was in reality the disease.

The bacteriological findings in several cases observed in the base hospital at Camp Lee seem to throw some light on the nature of the virus of mumps. Unfortunately this work was not started until the epidemic was almost over and there were few cases being sent in from camp. Our attention was first directed to the subject by the findings in the spinal fluid from a patient under treatment for mumps. This was one of a series of 9 patients who showed signs of a cerebral complication occurring during the course of the disease. A detailed report of these 9 cases is to appear elsewhere.[3] The spinal fluid showed uniformly a pleocytosis of the mononuclear type, very little or no globulin, a positive sugar reaction and a negative Wassermann test. Cultures and smears were negative in 8 cases. In one instance the fluid was opalescent and the findings the same as in the other fluids, except that smears showed numerous Gram-positive diplococci. No growth could be obtained on culture, and rabbits injected intraspinously were negative. All 9 patients exhibited clinically classical mumps, and the one case in which the organisms were found differed in no way from the other 8. The cocci were found in direct smear, so there was no chance of contamination. The fluid showed the same pathological features, so we see no reason to suppose that this patient had a secondary infection. It seems reasonable to conclude that the organism demonstrated in the spinal fluid was the one causing the primary infection, a parotitis.

After the finding of this organism in the spinal fluid we began to do blood cultures routinely on all cases of mumps on admission to the hospital. A total of twenty-five cultures was taken on eighteen patients. The cultures were made in dextrose and plain infusion bouillon. Nineteen cultures were sterile. Two were contaminated. Four cultures on three different patients showed a small Gram-positive diplococcus. The growth in broth was very slow. When transferred to blood-agar plates, organisms appeared in forty-eight hours in very small, dew-drop colonies. After several transplants it grew readily on all media. No pigment was produced on the blood-agar.

In the fifth case reported the blood cultures were negative, but the same diplococcus was grown from an inguinal gland, which became swollen subsequent to a very severe orchitis.

The histories of the patients from whom the organism was recovered are given in detail below.

[1] Arch. Int. Med., June, 1919.

CASE I.[4]—L. P., Pvt., Co. 2, 3d Bn., 155 D. B., aged twenty-five years, white, was admitted to the Base Hospital March 2, 1919, complaining of swelling of the left side of his face. He had had the usual exanthemata of childhood and pneumonia in 1918. On the day before admission he began to have pain and swelling of the left side of the face. Physical examination was negative except for swelling of the left parotid gland. His temperature was 100°, pulse 100 and respiration 20. On March 5 the right parotid became involved. His temperature returned to normal. On the next day he began to have a severe headache, which continued for two days, with temperature going as high as 103.6°. When seen on March 8 he was having severe headache and vomiting. He had no orchitis. The parotid swelling had practically disappeared. There was slight but definite stiffness of the neck and a slightly positive Kernig. The cranial nerves were negative. No deep reflexes could be obtained except the left biceps tendon reflex. The Babinski was negative. There was no clonus. Lumbar puncture showed an opalescent fluid under increased pressure. Following the puncture his temperature returned to normal and all symptoms rapidly cleared up. His recovery was uneventful. He was discharged to duty March 17, 1919. The spinal fluid showed 440 cells per c.mm., of which 100 per cent. were mononuclears. The sugar reaction was positive and a globulin test slightly positive. A direct smear showed Gram-positive cocci, but no growth was obtained on culture. Rabbits injected intraspinously with the fluid were negative.

CASE II.—G. A. S., Pvt. Co. A, 407 Res. Labor Bn., aged twenty-seven years, colored, was admitted to the hospital April 2, 1919, complaining of pain and swelling of both sides of the face. His family history was negative. He had had measles, chicken-pox, diphtheria and pneumonia. His present trouble had begun the day before admission and had gotten steadily worse. On admission there was extreme swelling of the parotid region on both sides. His temperature was 99.1°, pulse 84 and respiration 18. Physical examination was negative otherwise. The next day his temperature was 99.6°, and on April 5 it was 99.4°. Thereafter it was normal. A blood culture taken on the day of his admission showed a Gram-positive diplococcus. A second culture taken the following day revealed the same organism. The soldier had no complication and made an uneventful recovery. He was discharged to duty April 15, 1919.

CASE III.—D. S. B., Sgt. Util., Q.M.C., aged twenty-five years, white, was admitted to the hospital April 7, 1919, complaining of pain and swelling of both jaws. His family history was negative. He had had measles, chicken-pox and influenza. His present trouble had begun the day before admission, with pain and swelling at the angle of the jaw. Examination showed only swelling of both

[4] This case is included in the article on the Cerebral Complications of Mumps Arch. Int. Med., June, 1919.

parotids. His temperature was 101.3°. He continued to have fever as late as April 13, reaching 104° on April 11. Blood culture on the day of admission showed a Gram-positive diplococcus. He made an uneventful recovery and was sent to duty April 21, 1919.

CASE IV.—O. B. M., Sgt., Co. II, 3d Tr. Bn., aged twenty-three years, white, was admitted to the hospital February 6, 1919, suffering from acute tonsillitis. His family history was negative. He had measles and whooping-cough in childhood and influenza in January, 1919. He gave no history of mumps. The tonsillitis rapidly subsided, but he was held for observation for dizziness, which had developed suddenly while he was exercising on a horizontal bar in July, 1918. On March 6 he complained of joint pains, and it was noticed that his left submaxillary gland was swollen and there was also a swelling at the angle of his jaw on the right side. He had no fever. On March 21 his temperature was elevated and his left knee was swollen and tender. The submaxillaries were still enlarged. His ankles and wrists later became involved. His temperature was as high as 104°. On March 24 he began to have marked swelling and tenderness of the left testicle, which gradually subsided. There was a slight recurrence of the arthritis later. He was sent to a general hospital May 2, 1919, for further convalescence. A blood count done March 26 showed 4,900,000 red blood cells and 12,000 leukocytes, with a differential count of 72 per cent. polymorphonuclear neutrophiles, 19 per cent. small mononuclears, 8 per cent. large mononuclears and 1 per cent. transitionals. A blood culture taken on the same date showed a Gram-positive diplococcus. His Wassermann was negative. Morphologically and culturally this organism was just like the coccus isolated from the preceding cases.

CASE V.—S. J., Pvt., Prov. Gd. Co., aged twenty-three years, white, was admitted to the hospital April 3, 1919. His family history is unimportant. He had had measles, diphtheria and whooping-cough. He denied venereal infection. The day before admission he began to have pain and swelling at the angle of the jaw on both sides. His temperature was 99°, pulse 100 and respiration 24. Both parotids were swollen. Examination otherwise was negative. Blood culture yielded no growth. He continued to have fever, going as high as 103° on April 5. His temperature then fell for three days, reaching 104.1° on April 10, coincident with a severe orchitis on the right side. Following the orchitis the right inguinal glands gradually enlarged and became tender. These were at first discrete and rubbery, but an area of softening finally appeared in the center of the chain of glands. There was no urethral discharge at any time or any demonstrable lesion in the genital tract except the orchitis. The orchitis cleared up completely. He continued to have fever in the afternoon, usually between 99° and 100°. On May 20 the right inguinal glands were excised. Throughout the mass of glands there were areas of necrosis containing thick, greenish pus. Smears showed a few Gram-positive diplococci, which were grown in dex-

trose broth. One-fourth of a cubic centimeter of the broth culture was injected into the testicle of a rabbit. There was primary inflammation, which quickly subsided. On the eighth day the injected testicle began to swell and became about five times normal size. The swelling continued for four days. Cultures were made from a drop of fluid obtained by puncture of the swollen testicle, but no growth was obtained. The testicle gradually returned to normal size.

Major D. L. Harris, M.C., Chief of the Laboratory Service, makes the following report on the excised glands: "Examination of sections of this gland shows numerous foci of necrosis. Surrounding these areas there are large numbers of epithelioid cells and a few multinucleated giant cells. The cells have the peripheral arrangement commonly observed in tuberculosis. No tubercle bacilli could be found in the stained sections (alcohol fixation used), but the lesions resemble in all respects those found in tuberculosis."

Clinically, the condition did not suggest a tuberculous adenitis. It followed a severe orchitis directly, and there was no other demonstrable lesion in the area drained by this group of glands. We know that the mumps organism excites a mononuclear reaction, which is best shown perhaps in the pleocytosis of the spinal fluid in mumps meningitis when the cells are all mononuclears. A diplococcus was found in direct smear and the injection of the broth culture produced an orchitis in a rabbit. No tubercle bacilli could be found in sections. We believe this was a granulomatous lesion in the gland caused by the mumps organism.

Major Tasker Howard, M.C., Chief of the Medical Service, reports from this hospital three cases in which a meningo-encephalitis was the only manifestation of mumps. The spinal fluid from two of the patients showed a Gram-positive diplococcus on smear and culture identical with the organism described in this paper. A saline suspension of the culture from one spinal fluid was injected into the testicle of a rabbit. On the following day there was some swelling, which subsided quickly. Nine days later there was a marked orchitis. Smears from the testicle showed lymphocytes and Gram-positive diplococci, which were grown in culture.

SUMMARY. Five cases of mumps are reported in which a Gram-positive diplococcus was isolated from the spinal fluid, the blood and a lymph gland.

The injection of the organism into the testicle of a rabbit produced a severe orchitis in ten days.

These findings confirm the earlier reports of similar organisms from cases of mumps.

Mumps is probably caused by a Gram-positive diplococcus and not by a filterable virus.

I am indebted to Major Tasker Howard, M.C., Chief of the Medical Service, for the privilege of studying and reporting these cases, and to Private E. R. Brooks, M.D., U.S.A., of the laboratory, for making the cultures and the animal inoculations.

IS ESSENTIAL EPILEPSY A LIFE REACTION DISORDER?[1]

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The present, perhaps, may be considered a fitting moment and place to state, more or less briefly, some of the newer psychological observations of essential epilepsy, viewed largely as a life-reaction disease or syndrome occurring in particular types of individuals possessed of certain instinctive or inherent defects of character or emotional make-up. We shall discuss (1) the so-called epileptic character and its development; (2) the causes of the epileptic fit; (3) the nature and meaning of the fit itself; (4) the rational deductions in care and treatment of epilepsy drawn from such a viewpoint and study.

For the purposes of this paper, essential epilepsy is meant to embrace that type of the disorder which is exclusive of the so-called organic epilepsies and those suffering from definite physical lesions or disfunctions of the viscera which secondarily induce the disease, thus leaving an apparently sound and healthy individual having epileptic attacks of apparent idiopathic origin. A life-reaction disorder is meant to embrace that type of phenomenon which may be compared to a state of rage or anger as seen in bad-tempered individuals or excessive emotionalism as seen in the hysteric and the like.

From ancient times the essential epileptic has been considered a peculiar type of individual. The salient features of the so-called epileptic personality in its most exquisite and classic evolution are egocentricity, extreme supersensitiveness, marked emotional poverty and rigidity of ideation and mentation. For years this character type has been supposed to develop in direct proportion to the severity and frequency of epileptic seizures upon which it has been assumed to depend more or less directly. Careful analysis has, however, shown that while the most glaring character faults and mental deterioration may be seen in those epileptics with frequent and severe seizures, this is by no means the invariable rule, there being many defects of instincts and evidences of severe habit deterioration in epileptics with but mild seizures. Indeed, many epileptics may undergo increasing impairment in seizure frequency and severity independent of sedatives, and yet such individuals may show by life reactions as well as by psychological tests that the deterioration is progressive and marked. The reverse of this statement may also be shown. In consequence we have come to realize that while the severity and seizure frequency on the one

[1] Read before the American Psychopathologicpl Association, Atlantic City, June 18, 1919.

hand, and instinctive defects and mental deterioration on the other, may be to some degree coincident, they bear no essential causal relation. On the contrary both syndromes are the expressions of a deteriorating process not summated in fits or their congeners. For several years I have studied a large series of essential epileptics as to their primary mental endowment before fits occurred. It was found that in practically all there was nothing wanting in mental makeup not seen in the frank and veteran epileptic. The character faults varied, perhaps, in the amount and degree present in such potential states before seizures, but the character defects were sufficiently glaring to mark such individuals as pathological personalities portending a possible epilepsy in later life.

The Detailed Development of the Epileptic Character. Inasmuch as the life reactions of the epileptic character are the distinguishing factors of the makeup, we may sketch the defects of maladjustment at the several epochal levels of life stress. At birth the potential epileptic child frequently has periods of meaningless crying. This extra-irritability and sensitiveness is so pathological that it rarely fails of detection and record. For instance, one history states the child "was considered a nervous and irritable child from the day of birth." A second "fretted continually at the contact of rough clothing," while a third "was nervous and persisted in infantile demands long after weaning." A fourth "cried continuously the first three months," although nothing physically abnormal could be detected. One infant nearly went into spasms at the sound of an air-brake. Still another had to be rocked continuously and slept only during this care. The next important sequence in such a character is its non-pliability in being taught nursery ethics—that is, obedience and proper daily deportment in the home. These behavior defects are usually independent of purely intellectual and physical ones, and these infants sit up, creep, talk and walk at the usual ages. Indeed, in not a few the physical and the intellectual development seem accelerated and certainly are hyperactive. Extreme lability of mood is a frequent factor. One moment contented and the next irritable beyond power of appeasement is often noted. The consecutiveness of purpose in play and capacity to be amused is short, requiring the constant attention of the parent and a variety of interest appeal. Of one such epileptic it is stated that "he seems never to have developed out of his infantile ways; his rigid attitude of mind as a child is still in evidence in his adult life, and now he has fits added." Tantrum episodes even under the mildest discipline are most common in these difficult children. Their maladaptive defects are soon shown in their association with other children. They demand the play to be arranged to suit them; a game must be played a certain way; it must be continued or stopped as they direct. Their likes and dislikes are extreme. In the school

under an impartial discipline these potential epileptics show the most marked traits. The mood is inconstant, the interest and attention continually vary, and hence their more purely intellectual processes often show wide dissimilarities in evolution. Extremely brilliant in some subjects and quite ignorant in others is the general rule. Because of their extreme nervousness and inability to conform to school routine, many children fail physically and mentally and cannot take on the normal school training. Some are privately tutored; others are exempted from school discipline and routine except for short periods. Such scholars often appear pale and haggard, the pupils of the eyes are dilated, and they grow lethargic and sullen or sit day-dreaming and yawn, although not really sleepy. They grow intolerant of the school and often rebel at its confining and exacting demands. Thus in infancy and early childhood the instinctive defect of the ego fails of proper sublimation or extraversion; the adjustment to the social and physical environment is incomplete and unsatisfying, and, thrown back upon itself, in consequence there is a reinflation of self-importance and sensitiveness. Childhood, therefore, is a fruitful period for new and unbearable stresses, and sequential epileptic attacks often occur in one predisposed. The next stressful period is at puberty; here the dissolution of the oftentimes irksome home ties may release some from the galling exactions of home discipline, but most frequently, as in the departure for school, with its exactions in deportment, we find the puberty adjustment to work and social demands increasingly onerous. The potential epileptic is not willing to take on a proper attitude of apprenticeship. He has the innate instability of the constitutional inferior, but the good-natured indifference of the latter is not his attitude; his feelings are easily hurt, he has illy defined paranoid persecutions which cause him frequently to react with violence, insolence and hatred. He has attacks of rages, sullen moods and disspirited acquiescence in plans and undertakings. The lack of good fellowship renders him incapable of coöperative teamwork. The potential epileptic admires coöperation and the doing of big things in the abstract, but the requirements of interdependence and subordination to the main purpose galls and irritates him beyond endurance. He often develops fugues and tries a number of precarious jobs, often interspersed with excesses of self-indulgence. The potential epileptic during early adolescence begins already to present an odd mixture of primary defects of instincts plus a beginning deterioration of the higher capabilities of social adjustments known as habit deterioration. In part the latter is protective—that is, under the extreme stresses of this period he may ease off the stress by lowering or evading the exactions of precise behavior and deportment. Thus instead of presenting fits for a time he may take on various dissipations, alcohol, sexual excesses, wanderlust, gambling and licentious practices. The

explosive and impulsive character, the hatred and bitterness of the manner in which the acts are perpetrated, or underneath the seeming callous indifference and total lack of feeling with which the potential epileptic perpetrates these social delinquencies, is revealed the crudity and deep-rooted sadistic impulse of the epileptic character. With no real or intimate friends the potential epileptic holds himself aloof from the demands of the common sacrifice of self and the mutual dependence of social custom. He is a free lance, able and usually anxious to work his own will upon the world. If gifted with extraordinary intellectual endowments he may succeed for a time and make satisfactory progress toward his goal, but just short of it his egotism and ambition are often fired to new and impossible ends; when the whole scheme seems to him within final consummation some small trick of fortune adds the last burden of stress upon his mental and physical health and the individual breaks into frank manifestations of his disorder.

Freed in greater part from the trammels of social concern and demand, the intellectual efforts of the potential epileptic work with less stress than the normal, but in the final and more advanced consummation of his task the social customs of the family, friends and society itself fail to add their small but modifying influence as a directing force to the effort. In consequence new and unforeseen hindrances are added which in turn reduce the mental and physical invulnerability to the minimum, and at such defective periods some physical stress which at a more favorable time would be quite negligible appears as the precipitator of the frank disorder. Thus one learns to discount the common precipitating cause of the epileptic attack; such obvious studies are but surface ploughing of the etiological field in epilepsy. One is apt to think that inasmuch as epilepsy is essentially a disease of early life the great majority are unmarried because the state in itself bars marriage, but in the vast majority the reason is by no means so casual. It is really because the epileptic is rarely equipped in essential character makeup for marriage. Emotionally and sexually he rarely develops beyond the level of puberty and fails in capacity to attain adult love. Naturally this is to be expected in that the latter demands self-subordination and sacrifice, and above all a tenderness of feeling which is conspicuously lacking in the potential epileptic. In view of the foregoing it is evident that marriage increases demands socially as well as economically and makes not a few potentials break out in attacks. At the threshold of life the vast majority of potential epileptics break before or just at this period, which is the point of maximum stress. Almost all potential epileptics long before their disorder becomes at all acutely manifest, show increasing slowness and a diminished capacity for sustained employment. They show extra fatigue and diminished interest—a partly protective mechanism. A tenacious, consistent, all-around emotional

development in a life-work seems impossible in the vast majority. They work fairly well for a time, with plenty of emotional appeal, lavish praise and constant change—all essentially infantile traits of character—but in the end fail to do a thoroughly competent life-work.

THE NATURE AND MEANING OF THE CONVULSION. The muscular convulsion may be explained hypothetically in two ways, or a combination of the two explanations may be desirable. We know the convulsive part of the fit in its severer and cruder aspects is comparable to the impulsive movements of the infant. The impulsive fetal movements begin about the twelfth week of gestation, hence the brain cannot be involved *per se* in their genesis; further, it is known that brainless embryos possess impulsions. There is a short period just before birth in which the amniotic fluid and the uterine wall greatly inhibit the free play of these impulsive movements, but they begin again with renewed activity in the newly born and are slowly inhibited by voluntary control at the end of the nursing period. We do not know just how the impulsive movements are incited further than to surmise that, being of the first, simplest and ontogenetic type of activities of the developing organism, their incitor is from motor centers of the lower order. In these latter structures are stored up a certain quantity of potential energy which is transformed into actual energy by the blood and lymph stream. With the increasing tissue growth and tension engendered thereby this energy finds its outlet in the random movements of the fetus and the infant, and their exaggerated distorted presence is seen in the grand mal convulsion of epileptics. Time prevents us from outlining more in detail the essential distinguishing characteristics of the impulsive from the instinctive, reflex and conscious or ideational movements of the infant; this has been done most carefully by Preyer and later correlated into a recent study by Canestrini. Suffice it to say the newer studies on the meaning of the convulsive part of the epileptic fit make careful analysis of all the impulsive movements of the nursling doubly necessary. It will then be found desirable to note their exact relationship in reference to the psychosexual development and its defects as shown in the infantilism of the epileptic.

As might be expected the number of the impulsive movements is not great. They may be schematized as those of outstretching and bending the arms and legs in the newly born. The movements are sometimes so quick as to resemble the cloni of a fit. They may be slow, then fast and finally end in cloni. Even in healthy infants they may be so slow as to resemble the tetanoid spasm of a beginning focal seizure. Preyer speaks of the muscles involved in the impulsive acts as possessing such a slow, crawling movement that the acts present a striking resemblance to the extension and flexion of the limbs of animals waking from their winter sleep.

Such animals, like sleeping children, seen even in the first half of the second year make genuine fetal movements which often look as though they were directed against some invisible resistance. This all suggests many of the striking impressions one gains in observing the convulsions of epileptics. Convulsive motions in the infantile impulsions are, however, not generally so frequent in sleep as slow contractions. The latter are frequently attended by spreading and bending of the fingers which in turn become the rarer toward the end of the second year in all children of sound nervous systems. All these impulsive movements, in the hands especially, are asymmetrical in outline.

What are some of the depressors and incitors of these impulsive movements? Deep, profound and quiet sleep reduces them to the minimum. Satiation by food greatly curtails them. On the other hand a duplication of the intra-uterine state by the use of the warm bath encourages them. The movements are then usually slow and rather rhythmic and graceful. One may even see in them the beginning of an expression of pleasure. The face may join in the picture of contentment with slow asymmetric contortions, which semblance has an odd mixture of pleasure with more than a hint of displeasure. The greater part of the impulsions, however, are purposeless, senseless and asymmetric and are found over the entire body from the first day of birth. Writhing and twisting of the body are also frequent accompaniments to the movements of the face and extremities. Just as the infant sinks into deep sleep these impulsive movements slow down and the body usually comes to a state of rest in the fetal position. The fetal posture in the legs is kept up longer in advancing child life than that of the head and upper extremities. Many writers have called attention to the fact that no one could consciously duplicate these acts. Then, too, one is strikingly impressed that the infant and the epileptic alike are little fatigued by these most intense and persistent impulsions, which speaks strongly for the unconscious motivation in both their activities. Probably in both subjects the fund of reserve energy being so limited in scope is greater than that of the normal adult as ordinarily expressed in his daily activities. Biologically speaking we know that the essential vital energy of an individual is probably at its maximum at birth.

We are justified in considering the essential nucleus of the epileptic fit an infantile unconscious striving of displeasure-pleasure pursuit ending in the final goal of a return to infancy, attended by a loss of consciousness and a convulsion; that the convulsion is made up of and flows out of the general striving of the fetal and infantile tissues as expressed through the lower spinal centers in inducing simple and crude combinations of impulsive movements; that a study of the degree of development of unconscious infantile strivings in the emotional instincts, the desire for an infantile state

of omniscience, are paralleled by the kind and character of impulsive movements found in this infantile period of neuromuscular development. Therefore the two main settings in the epileptic fit, unconsciousness and convulsion, are psychical and physical correlates; lastly, that epilepsy in its essential pathogenesis is an error or arrest in this fundamental elaboration or development of the emotional life.

Having schematized the dynamic mechanism of the epileptic fit, we may note that the essential pathogenesis of the disorder as a whole is still to be attacked. Whether the latter rests upon an inheritance of certain psychic traits alone or whether there are certain somatic structural anomalies which do not permit proper psychosexual development into normal adult life one cannot say. I believe such studies, however, narrow the gap between such causes and their psychophysical expression in epilepsy; and finally, such observations must be of greatest aid in classifying the recoverable epileptics from the irrecoverable ones. It also points the way by which we may advance our therapeutics of the disease along the broadest biological lines of educational and moral treatment. In this connection one may note that MacCurdy has tentatively formulated the idea that the sudden loss of consciousness in epileptics liberates a muscular anarchy or "clotted mass of movement" of many different lower levels or physiologically controlled centers in the brain and spinal cord, and that the convulsive part of the fit is a released neuromuscular mechanism or series of mechanisms entirely secondary to the loss of consciousness, the main defect of the epileptic state. He holds the same fundamental postulate as to the psychological meaning of the epileptic fit as we have formulated it.

The Psychological Causes of the Loss of Consciousness. Given the inherent defect of makeup just detailed, it is easy to comprehend how all forms of undue physical and mental stress may operate deleteriously upon the epileptic. The gradations of epileptic reactions vary from day-dreaming, lethargies, petulence, sullenness and outbursts of impatience and temper beyond the casual, until there succeeds a series of petit mal attacks or a severe grand mal, when the lowering skies in the epileptic's life are dispelled for a time until the stresses again accumulate to an explosive level. So long as normal consciousness is maintained the stress may work its evil consequence in ways well known to all. The epileptic reaction from its mildest to its severest manifestation is really a protection, for it obliterates reality and reduces the subject to the lowest level of organic response—that of a comatose state. Hence the fit is really a protective mechanism, psychologically considered at least. It withdraws or reduces the subject's attachment and adjustments to reality. It dispels an intolerable demand and the epileptic retreats to a state of harmony and peace. In the

retreat after incomplete attacks we frequently encounter unconscious strivings and conflicts that have baffled the subject. So exogenous causes, physical and mental in character, slight as they may seem to be, precipitate a conflict which springs the fit-gun, and a series of conflicts of different levels in the unconscious are exposed until after the severe grand mal attack the subject is reduced to the lowest level, comparable to earliest infantile life. When this hypothesis was enunciated a few years ago it was as yet uncorroborated by exact data, but since that time innumerable studies bearing out every contention of the mechanism have been deduced. Thus we find in the mild and transitory deliria of the automatic phase after petit mal attacks the subject may say or do certain things which may be pieced together and minutely analyzed. Like the mental content in manic states or drug and fever deliria these spontaneous productions have to do with the conflicts of every-day life. Then appear the successive deeper levels of emotional strivings and conflicts. For instance, at first the epileptic attempts to rid himself of an onerous task or unpleasant companions; sexual strivings are uncovered and in the deepest level he has made a retreat to the home, is in the cradle or the mother's arms, etc.

THERAPEUTIC DEDUCTIONS. Anyone following this therapeutic procedure should bear in mind that epilepsy from its very nature is a deteriorating disorder physically and mentally, and if it be allowed to progress it steadily lowers the capacity of the individual to make new and difficult adaptations. Hence any treatment which is based upon widening the plan of living is in itself bound to be very stressful. At first one cannot put this extra strain upon the epileptic without entailing more attacks than before. Frequently the plan of analysis given here must be undertaken for short periods only (days or weeks), and then the patient should be allowed to rest in his newly acquired position until he thoroughly accustoms himself to it, when more advanced work may be again undertaken. If the same content in the automatic state repeatedly returns, one must conclude that the special conflict about which the desire in the content groups itself is so basic that mere analysis will not set it free. Then a practical system for eliminating this defect must be instituted. Sooner or later one finds that simple analytical talks are the supplemental guides to more definite methods of training out the personality defect. The susceptibility to meet this reëducation will give a just estimate of the prognosis in the individual case. It has also been found that coincident with a gradual disappearance of epileptic reactions, as shown in the fits, *per se*, there must be a corresponding increase in capacity for work and other spontaneous living interests. Usually these clinical evidences of betterment are heralded by a shortening in the reaction time and a lessening of perseveration. The mere cessation of attacks, especially under sedatives, without corresponding improve-

ment in the psychological tests, is an indication that the underlying deteriorating disorder has not as yet been favorably modified and that the epilepsy may in course of time be expected to break out again after a temporary arrest.

In conclusion, one may say that a psychological study of the mental content in epileptics, both conscious and unconscious, demonstrates: (1) the depth of unconscious regression; (2) the special types of conflict which the epileptic has and the way he tries to solve them; (3) the specific type of primary defect in his endowment. Its therapeutic value in addition is (4) to furnish a specific point of analytical attack by simple explanatory talks; and (5) to show more definitely the type of special education which should be adopted for each individual patient.

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BLOOD TRANSFUSION.

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Blood transfusion as it is practised today in the foremost hospitals is one of the greatest therapeutic advances in the last decade. The indirect methods which have been introduced are not only more practical procedures, but they also produce the desired clinical results. The technic of direct transfusion is an art which requires the skill of the best surgeons, and even in their hands it is not always successful, whereas the indirect methods can be performed by anyone who has a competent laboratory at hand and is familiar with venipuncture. To Dr. E. Lindeman[1] is due the credit of reviving and perfecting the syringe cannula method which was used by von Ziemssen[2] in 1892. Since Dr. Lindeman's introduction of the

[1] Am. Jour. Dis. Children, 1913, vi, 28.

[2] München. med. Wchnschr., 1892, No. 19, p. 323.

indirect procedure numerous other methods have been introduced including the citrate, the two-way stop-cock methods of Unger,[3] Freund[4] and Kush[5] and the paraffin tube of Kimpton and Brown.[6] No doubt some of these were known and practiced in a limited manner before 1913, but they were not universally adopted. No one can deny the advantages of the indirect methods when it is considered that the operator is always aware of the exact amount of blood that the patient is receiving, that repeated transfusions can be performed on the same patient and that the donor is not submitted to an extensive operation.

Not only was it necessary to perfect the technic of the operation, but it was also necessary to devise some means of determining compatible bloods, and before this was accomplished transfusion was always surrounded by an element of danger. Moss and Ottenberg have been working independently on the isohemolysins and iso-agglutinins in human blood for the past ten years, and today after properly carrying out the laboratory examinations suggested by these investigators, one may perform a transfusion without fear of an accident to the patient.

INDICATIONS. On account of the ease with which transfusion is performed it is suggested for almost all the ills that man is heir to. It has, however, certain definite and real indications wherein it is the one therapeutic agent which saves life, and it has others in which its usefulness is largely that of a supportive measure, and when combined with surgical or medical treatment the results are very gratifying. In 1915 Libman and Ottenberg[7] reported 212 transfusions and fully discussed the results and indications.

Leisrink (quoted from Pemberton[8]) says that "transfusion is indicated in all those conditions in which the blood in quality and quantity is so altered that it is unfit to fulfil its physiological duties."

My experience has been very largely in cases of acute hemorrhage, and to more than one patient it has proved a life-saving device by carrying them over the critical period of air hunger and collapse. Recently a case of postpartum hemorrhage and inversion of the uterus was admitted to the hospital. There was no radial pulse, and when transfusion began the respirations were at the rate of four to six per minute. After 200 c.c. were injected the patient stopped breathing and no heart-sounds were heard with a stethoscope. However, the operation was continued on the presumption that when the heart became filled with blood it would be stimulated to more forcible contractions, as it was probably contracting weakly, although no sounds were audible. After 400 c.c. had been

[3] Jour. Am. Med. Assn., 1917, lxix, 2159.
[4] Jour. Michigan Med. Soc., 1913, xii, 459.
[5] Jour. Am. Med. Assn., lxv, 1180.
[6] Ibid., 1913, lxi, 117.
[7] AM. JOUR. MED. SC., 1915, cl, 36.
[8] Surg., Gynec. and Obst., 1919, xxviii, 262.

given the heart could again be heard and respiration was reëstablished. The transfusion was continued until the donor fainted, when 1200 c.c. of normal saline solution was introduced. This procedure kept the patient alive for three or four hours until another donor was secured. Eight hundred cubic centimeters of blood were injected at the second transfusion and the general condition of the patient gradually improved. Thereafter the clinical course was uneventful and she was discharged from the hospital as recovered in two weeks.

In some cases of shock transfusion is valuable, for, according to Cannon's hypothesis, shock is due to a diminution in the normal alkalinity of the blood caused by deficient oxidation, secondary to loss of red blood corpuscles, cardiac weakness and low blood-pressure. In such cases the addition of fresh normal blood will restore the alkalinity and relieve the existing condition.

Many times I have seen the introduction of 500 to 1000 c.c. of blood shorten convalescence and entirely change the clinical course of patients suffering with marked secondary anemia, due to uterine hemorrhage and localized pelvic sepsis. In these individuals it acts as a supportive measure and gives the patient some means of combating the infection. On the other hand in cases of general peritonitis, puerperal bacteremia and septic thrombophlebitis of the pelvic veins transfusion has a small or transitory effect, for normal serum has little bactericidal power.

As a preoperative procedure in cases of uterine fibromata, gastric ulcer and many other conditions in which the extensive anemia does not permit immediate operative interference, transfusion has an ideal place, and the necessary surgical treatment can be subsequently carried out without endangering life. It is true, however, that in acute hemorrhage such as ectopic pregnancy, placenta previa and rupture of the uterus it is well to secure all bleeding-points first or be prepared to do so, for on more than one occasion I have seen cases which have stopped bleeding begin again after the introduction of 500 c.c. of blood.

Transfusion acts as a specific in hemophilia and hemorrhage of the newborn, for whole blood supplies the human organism at once with all the substances of the plasma, cells and platelets necessary to elaborate thrombin at a distal bleeding-point. But, however, in the newborn transfusion is a highly technical process on account of the size of the superficial veins. Even the superior longitudinal sinus as a site of injection has its disadvantages, for more than one operator has injected blood beneath the dura until the infant ceased or almost ceased to breathe.

In severe secondary anemia of various incurable diseases transfusion overcomes the annoying symptoms and prolongs life for a certain period of time, but these periods tend to become shorter and the patient ultimately succumbs to the original disease. Even

if life can be prolonged for a few months or years, transfusion is well worth while.

Transfusion is one of the best remedies we have for pernicious anemia, for although it probably never cures this disease it may repeatedly initiate remissions in many of the chronic cases and these remissions often last much longer than the normal remissions. In my opinion it is advisable to transfuse patients suffering from both primary and secondary anemia earlier than has been the usual custom and not wait until the hemoglobin is below 30 or 40 per cent. and the red cells below 2,000,000. By so doing the patient will avoid for some time that severe grade of anemia which produces exhausting effects and extensive degeneration of the parenchymatous organs.

Transfusion is occasionally of some value as an additional therapeutic aid in typhoid fever, prolonged suppurative cases and certain medical conditions, associated with a marked or moderate grade of anemia in which some such agent is necessary to throw the balance in favor of the patient rather than the disease.

ISOHEMOLYSINS AND ISO-AGGLUTININS. Before there was any knowledge of iso-agglutinins or isohemolysins certain definite clinical reactions took place in the patient during or after transfusion which were characterized by severe symptoms and occasionally death. This phenomenon, which did not occur in all transfusions, was attributed to the introduction of air into the veins.

It has been shown by Ottenberg and Kaliski[9] that these severe reactions are due either to isohemolysins or iso-agglutinins, or both in the blood serum of the donor and the recipient, and that by making careful preliminary blood examinations these accidents can be absolutely avoided. Moss and Ottenberg appear to be somewhat divided as to the occurrence of hemolysins in human blood. Moss[10] says that isohemolysins are probably always preceded or accompanied by iso-agglutinins, both in health and disease, and cited but two instances in 100 examinations in which the isohemolysins occurred independently of iso-agglutinins. This result he attributed to faulty technic. Many workers have followed Moss's hypothesis, and in making the preliminary tests have examined blood only for iso-agglutinins.

Ottenberg and Kaliski[11] say that hemolysis of one human blood by another is a pathological phenomenon and has demonstrated it in a variety of diseases, while Moss[12] states that isohemolysins occur in about 25 per cent. of human beings. It is therefore quite apparent that both investigators differ as to the occurrence of hemolysins in human blood in health and disease. After the examination of many specimens of blood it has occurred to me that as long as the tests are confined to normal individuals or to those who have suffered from

[9] Jour. Am. Med. Assn., 1913, lxi, 2138.
[10] Johns Hopkins Bull., 1910, xxi, 64.
[11] Loc. cit.
[12] Loc. cit.

acute hemorrhage the group agglutination reactions of Moss are quite sufficient. When examining the blood of patients suffering from a chronic disease it is well to make the additional test for hemolysins, as these hemolysins may be developed in the course of that particular disease, and in some instances they may be autohemolysins.

Iso-agglutinins are inherited, occur in normal bloods and can be readily tested for by modern methods. Landsteiner[13] and Shattuck,[14] working independently, in 1901 discovered iso-agglutination of human red blood cells, and Landsteiner divided human beings into three groups according to the inter-agglutination reactions of their bloods. In 1907 Jansky[15] proved that human beings fall into four groups, and this was later confirmed by Moss.[16] Since then the technic of determining the group to which an individual belongs has been simplified by Brem,[17] Sanford[18] and Moss,[19] and the determination can be made in a few minutes.

It has been suggested by some observers that individuals may change their groups after repeated transfusions, but it has been my experience that as long as the donor and recipient have been of the same group it is very unlikely that any change takes place. On the other hand if agglutinable cells are injected into a patient it is quite possible to assume that new agglutinins will be formed. In fact, Ottenberg, Kaliski and Friedman[20] have shown that dogs transfused with agglutinable cells will apparently develop iso-agglutinins *de novo*, but this will not occur when the injected cells are not agglutinable.

Ottenberg and Kaliski[21] have demonstrated by blood smears during and after transfusion, in which the donor's cells were agglutinated by the recipient's serum, that phagocytosis of red blood cells occurred, but in cases in which the serum of the donor was agglutinable for the cells of the patient no phagocytosis was observed. This is due to the dilution of the agglutinins in the serum of the donor by the serum of the recipient and has led to the practice of using Group IV as the universal donor, inasmuch as the serum of Group IV agglutinates the cells of Groups I, II and III, and Group I as the universal recipient, as its serum does not agglutinate any corpuscles. These facts, together with the occasional occurrence of a serum weak in agglutinins, are responsible for the few reactions which occur when no preliminary tests are made.

[13] Centralbl. f. Bacteriol, 1900, xxviii, 357; Wein. klin. Wchnschr., 1901, xiv, 1132.
[14] Jour. Path. and Bacteriol., 1900, vi, 303.
[15] Abst. Jahresb. u. d. Leistung u. Fortschr. a. d. Geb. d. Neurol. u. Psychiat., 1907, xi, 1092.
[16] Johns Hopkins Bulletin, 1910, xxi, 64.
[17] Jour. Am. Med. Assn., 1916, lxvii, 190.
[18] Ibid. p. 808.
[19] Ibid., 1917, lxviii, 1905.
[20] Jour. Med. Research, 1913, xxviii, 141.
[21] Jour.Am. Med. Assn., 1913, lxi, 2138.

DONORS. As far as possible donors should be strong, healthy, muscular individuals without a nervous or timid temperament, otherwise the operation may be terminated earlier than is desired on account of an attack of syncope. Wassermann tests and a physical examination are made on all donors before each transfusion regardless of the fact that they have been examined on previous occasions. Syphilis has been transmitted on more than one occasion in this way and in the examination of 150 donors I have obtained six strongly positive reactions. Even after explaining the seriousness of transmitting this disease, donors have denied a history of the infection in every instance.

It has been the practice of the laboratory during the past three years to have on file a number of donors in each group, and when the emergency arises the patient is grouped and a suitable donor is reached by telephone or telegraph. On his arrival he is again tested for iso-agglutinins and isohemolysins and a Wassermann is made in order to be doubly sure that he is the most suitable candidate. Agglutination tests are made according to the latest methods of Moss,[22] and if there is time this is confirmed by Brem's[23] method. In using the group method one is less liable to overlook a serum weak in agglutinins, as this mistake occasionally occurs when the serum and cells of the patient are tested against the serum and cells of the donor according to the method of Lee.[24] Brem[25] recommends the use of Group II serum and cells as a standard, but it is of greater advantage to make the test with Group III serum, as 40 per cent. of individuals are in Group II and only 7 per cent. in Group III. Therefore, cross-agglutination will occur almost six times as often in testing unknown bloods. Examination is also made for hemolysins if it is thought necessary after a consideration of the patient's history. When the group system was first introduced hemolysin reactions were always made as a check, but this was soon found unnecessary in patients who were acutely ill from hemorrhage or sepsis. With the Moss method there is no emergency so great but that the operator can be reasonably assured that he is transfusing patients with compatible bloods. Very often in the hospital service patients are admitted in a serious condition after hemorrhage and prompt action must be taken. The patient, the friends and the hospital porters are grouped while the necessary preparations are being made for the operation. As far as possible only individuals of the same group are transfused, and when this cannot be done a Group IV donor is selected.

The amount of blood taken from the donor depends on the weight and condition of the patient, the weight of the donor and the indication for which the operation is performed. Inasmuch as the

[22] Jour. Am. Med. Assn., 1917, lxviii, 1905.
[23] Ibid., 1916, lxvii, 190.
[24] British Med. Jour., 1917, ii, 682.
[25] Jour. Am. Med. Assn., 1916, lxvii, 190.

blood in the human organism is about one-nineteenth of the body weight, and a man weighing 170 to 190 pounds would have from 9 to 10 pounds of blood, one-fifth to one-fourth of this amount could be transfused without any unfortunate result. However, it is always well to watch the donor for such symptoms as yawning, sweating and a lowering or elevation of the pulse-rate, as under such conditions it is advisable to stop. Very occasionally they go into collapse, from which they recover in a short time under appropriate treatment. This is not a pleasant feature and can always be avoided by carefully observing the donor when the amount transused approaches 1000 c.c.

At the present time professional donors are repeatedly submitting themselves for transfusion when they are not physically fit. This can be readily determined by taking the percentage of hemoglobin and by bleeding them into a test-tube and estimating the relative volume of solid and fluid constituents of the blood. The blood of one who has been repeatedly bled and is suffering from secondary anemia always shows a much larger proportion of serum than cells; this type would certainly not be the most beneficial to the patient. Some donors are used as often as every six weeks, but an interval of from three to four months is more desirable in most individuals.

Recipient. Unlike the donor we have no choice in selecting the recipient, but if time permits they are placed on a Karrel diet (900 c.c. of milk) for twenty-four to forty-eight hours before the operation, so that the transfused blood is less liable to overburden the heart. A mild cathartic or low enema is also given depending upon the physical condition of the patient, and occasionally a hypodermic of morphin one-half hour before the operation relieves the nervous excitement and slight pain associated at times with the procedure.

Methods. At the present time physicians interested in transfusion differ widely in their opinions as to the relative value of modified and unmodified blood. The citrate method has gained its popularity on account of the facility with which it is performed, but there is no reason to believe that it is as beneficial to the patient as the unmodified blood which is not subjected to a chemical change and which is out of the body such a short time. It is indeed quite true that citrated blood is entirely efficient in patients suffering from acute hemorrhage when volume only is needed, but with patients who have had a severe anemia for some time and are in poor physical condition the method which will accomplish the best results with the least possible tax on the already poorly functionating organs of the patient is the one to select.

The syringe cannula method of Lindeman,[26] where the operator,

[26] Am. Jour. Dis. Children, 1913, vi, 28.

assistant and nurse work together perfectly, is the nearest approach to a direct transfusion that can be obtained, and therefore the advantages of both the direct and indirect methods are combined. On the other hand with poor teamwork it can be made an absolute failure; thus it is very important to have the same assistants at every transfusion in order to be assured of the highest type of efficiency.

Inasmuch as the citrate method can be performed by one individual it is adaptable to emergency cases and to cases outside of an institution. Drinker and Brittingham[27] have reported several transfusions using different methods and make the impartial statement that it would seem that both the syringe cannula and the paraffin tube methods offer fewer reactions than the citrate. Clowes[28] has called attention to the similarity of sodium chloride and sodium citrate in their general effect on protoplasm. The difference between the salts is a function of the anion and the citrate is infinitely more toxic than the chloride no matter what the test material. The choice of the method depends upon the means at hand, and, whenever possible, the syringe cannula technic is to be preferred because it is the best method we have of injecting the same kind of blood that is already circulating in the vessels of the recipient.

Report of Cases. Since the introduction of indirect transfusion I have performed the operation 100 times on 79 cases, 81 by the syringe cannula technic and 19 in which sodium citrate was used as the anticoagulant. The cases of acute hemorrhage and sepsis occurred in the obstetrical service of the Lying-in Hospital and the chronic cases were transfused at home.

CONDITIONS FOR WHICH TRANSFUSION HAS BEEN PERFORMED.

Disease.	No. of patients.	No. of transfusions.	Died.	Recovered	Improved.	Not improved.
Hemorrhage	28	30	6	22		
Hemorrhage & pelvic sepsis	28	28	..	28		
Sepsis (general peritonitis, bacteremia and septic thrombophlebitis)	7	12	6	1		
Secondary anemia	8	10	..	..	6	2
Pernicious anemia	3	14	..	..	3	
Banti's disease	1	2	..	..	1	
Toxemia of pregnancy	4	4	2	2		

The fourteen deaths in this series, with the exception of one case which will be explained, were all due to the disease from which they were suffering and were not a result of the transfusion.

[27] Arch. Int. Med., 1919, xxiii, 133.
[28] Jour. Phys. Chem., 1916, xx, 407.

Under "Indications" I have already discussed the results obtained in the majority of these conditions, but I desire to mention one case in more detail in order to demonstrate the marked temporary improvement that does occur quite occasionally in patients suffering from chronic anemia. This patient has pernicious anemia and has been transfused nine times. Before each transfusion the physical condition was desperate, but after the injection of 1000 c.c. of blood the annoying noise in the head disappeared, the cough and subcutaneous edema cleared up and the appetite returned. Whereas before the transfusion the outlook was that of a fatal termination in a few days or weeks, while afterward this patient took a new lease on life and became interested in affairs even to the extent of returning to business. This result is due to the increase in the volume of blood and to the stimulation of the hematopoietic organs, but ultimately the hematopoietic organs do not respond to this stimulation and the patient depends entirely upon the mechanical action of the blood introduced which is of short duration. Occasionally it is necessary to transfuse cases at weekly intervals in order to get the blood up to a point where it will remain at a constant level for some time.

Reactions. A severe reaction with all the classical symptoms of hemolysis occurred early in my experience after an emergency transfusion for postpartum hemorrhage, but before which no examination for hemolysins and agglutinins were made. In no other case has there been any reaction due to hemolysis or agglutination, and I attribute this to the care with which the donors have been selected. I am surprised, after reading the protocols of some of the later articles in which serious reactions are described, for these have undoubtedly been due to careless laboratory work and in most instances it is very probable that the tests have not been made or supervised by the same individual that did the transfusion. Contrary to the conclusion of Sydenstricker, Mason and Rivers,[29] repeated transfusions in pernicious anemia can be done without danger to the patient if due care and patience are taken in selecting the donor.

Mild reactions characterized by a slight chill, rise of temperature and vomiting have occurred in a certain percentage of the series, but these were all transitory and passed off in twelve to twenty-four hours. The more perfect the technic of the syringe cannula method the less often will these so-called mild reactions occur. The careful and thorough washing of the syringes, the filling and emptying of the syringes and the length of time the blood is outside the body are small details which, if not carried out, may give rise to these reactions and establish the platelet and the anaphylotoxin hypotheses.

[29] Jour. Am. Med. Assn., 1917, lxviii, 1677.

CHANGES IN THE BLOOD FOLLOWING TRANSFUSION. The relation between the amount of blood transfused and the blood count afterward is a variable feature and is undoubtedly connected in some way with the condition of the individual patient at the time the transfusion is performed. A review of the protocols in an article by Huck[30] shows that in pernicious anemia the increase in red blood cells varied from 404,000 after a transfusion of 1250 c.c. to 1,784,000 after 750 c.c. in twenty-four hours. Huck's results after a series of observations is that, "in general, following the injection of blood there was an immediate increase in the red cell count. In some cases the initial increase continued for several hours, usually falling so that at the end of twenty-four hours the count had fallen to approximately where it was before transfusion. In other cases, however, there was a marked increase at the end of twenty-four hours. In several instances after the injection of blood the count fell for a few hours and then rose slightly. The hemoglobin in most cases showed a uniform rise following transfusion, usually reaching its maximum at the end of twenty-four hours. In practically every case there was some increase in the number of leukocytes." He concludes by saying that "the introduction of blood raises the count, that the effect is essentially a biological one involving the redistribution of blood in the body and its exact nature is not at present understood."

CONCLUSIONS. 1. The indirect method of transfusion, on account of its universal adoption, has saved the lives of many patients suffering from acute hemorrhage.

2. Patients suffering from primary and secondary anemia should be transfused early in the disease in order to obtain the best results.

3. Certain laboratory examinations are absolutely essential to the success of transfusion.

4. The syringe cannula method transfers blood from the donor to the recipient with the least possible physical or chemical change, and is therefore associated with fewer reactions.

5. No definite relation can be established between the amount of blood transfused and the blood count afterward.

I wish to thank Dr. E. D. Truesdell who has been associated with me in carrying on the teamwork necessary for the success of the Syringe Cannula Method.

[30] Johns Hopkins Bulletin, 1919, xxx, 63.

VACCINATION BY SUBCUTANEOUS INJECTION.

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In the spring of 1915, while attached to the Canadian Mounted Rifles as medical officer, I frequently discussed with Dr. George Hume, of Sherbrooke, the question of vaccination of troops by subcutaneous injection. He had done a few cases in this way, and before using this method upon the men of my unit I had it tried upon myself by Dr. Hume. I had been vaccinated ten times previously without success. Within three days my arm was sore and I went through all the general symptoms of successful vaccination.

Since then I have vaccinated hypodermically approximately 6000 men and quite a number of officers' children.

Method of Preparing Vaccine. It being impossible to procure vaccine in bulk, vaccine put up in the small capillary glass tubes was used in the majority of cases.

These vaccine tubes were first placed in methylated spirits for a few minutes, then withdrawn singly by surgically clean or gloved hands, the excess alcohol wiped off with sterile absorbent cotton, the ends broken off and lastly the sterile rubber bulb fixed to one end of the tube to blow out the vaccine into a sterile beaker. The vaccine generally shoots out of the tube into the beaker in the form of a small cylinder.

When the vaccine available was in small wax tubes the extreme end was first punctured with a sterile needle and the vaccine squeezed out by compressing the container.

From one-half to three-quarters of a tube of vaccine was used per individual. Sufficient sterile water was then added to the vaccine to make each injection equal to 1 c.c.

In private practice, or when one or two only are to be vaccinated, the vaccine may be prepared as an ordinary hypodermic injection, using vaccine instead of a drug.

Patients can be vaccinated with great rapidity. After preparation of the vaccine, four medical officers vaccinated 1100 in two and one-half hours by using 20 c.c. record syringes and injecting 1 c.c. into twenty successive men, changing the needle after each injection.

Technic of Injection. The arm was sterilized with iodin and the vaccine injected diagonally with a fine hypodermic needle and syringe into the subcutaneous tissues.

In a few cases, by mistake, the vaccine was injected intracutaneously.

Everything should be done with surgical cleanliness.

AFTER-EFFECTS OF INJECTION. The local reaction sets in usually between two and four days, but in a few cases the reaction is considerably delayed; and in one colonel's family three children were vaccinated and reaction did not appear until twelve, thirteen and fifteen days respectively.

The local reaction is much like that following antityphoid inoculation and just as variable in intensity. About 8 per cent. proved ineffective, showing but slight local reaction, not more than perhaps could have been accounted for by the iodin applied to the skin; in 70 per cent. (approximate only) there was a reaction similar to the usual reaction after antityphoid inoculation, *i. e.*, local swelling, heat, tenderness, slight pain and redness.

In a small percentage of cases the reaction was marked, causing swelling and edema of the elbow and, in a few cases, edema involving the whole arm and hand.

In every one of the 6000 cases vaccinated hypodermically by myself or under my supervision (for all of whom I myself prepared the vaccine for injection) the local condition subsided without any signs other than those of excessive local reaction.

After the seventh or tenth day the local swelling and induration subsided, leaving a hard nodule in the subcutaneous tissues, usually ill-defined at first, becoming later well-circumscribed and lasting for about one month. This is quite painless after the first acute reaction. The process differs in no respect from that of an antityphoid reaction, except that the onset is slower and the reaction spreads itself over several days.

The general symptoms vary in intensity and do not differ from those of ordinary vaccination.

INFECTION. In the 6000 cases quoted there was not one case of infection. This can be stated without question of doubt. The men were all soldiers who came directly under me and my medical officers for observation and for sick parade. They were all seen several times afterward, and in about 50 per cent. of the cases the vaccination was done at the same time or between the regular antityphoid inoculations. I saw one case of infection in another brigade; this was brought to my attention, and on close questioning it was found that there had been faulty technic. There was a punched-out ulcer about the size of a ten-cent piece, exposing the fascia. The ulcer healed without untoward result.

None of the 6000 required dressings, and the men were not exempted from anything but physical training and rifle drill.

A number were given light duty and a very small percentage were excused duty for a few days, owing to excessive local or general reaction. There were no hospital admissions.

In a few cases (about 10 altogether) the vaccine was injected intradermically, and about four or five days later there developed

the typical vesicular and pustular stages of ordinary vaccination, quite uncomplicated.

ADVANTAGES. 1. This is a clean surgical operation. If untoward results develop they are due to faulty technic.

2. There is no open wound and therefore dressings are not required.

3. Dangers of secondary infection are practically eliminated.

4. The percentage of positive reactions is very high.

5. In only a very small percentage of cases the local and general symptoms caused complete incapacity.

6. It is painless as compared with scarification.

7. Children undergo the hypodermic vaccination without any difficulty, owing to the rapidity with which the injection is carried out.

LABORATORY STUDIES IN INFLUENZA AT CAMP TRAVIS, TEXAS.

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WHEN the recent epidemic of influenza first appeared at Camp Travis it was thought advisable to ascertain what organisms were found most constantly in the nasopharyngeal and pulmonary secretions and exudates. Accordingly, cultures were made on defibrinated blood-agar plates of a selected number of patients who were stricken with the disease. In all, 868 cultures were studied and the bacteria isolated are given in the table below.

TABLE I.—NASOPHARYNGEAL CULTURES ON DEFIBRINATED BLOOD-AGAR PLATES.

Bacillus influenzæ	344 times
Streptococcus	108 "
Pneumococcus	83 "
Micrococcus catarrhalis	52 "
Staphylococcus	43 "
Bacillus hofmann	40 "
Streptococcus hemolyticus	22 "
Bacillus friedländer	22 "

The table shows that the Pfeiffer bacillus was found 344 times out of a total of 868 cases, in other words, the organism was isolated from the throats of 39 per cent. of the patients.

BRONCHOPNEUMONIA. The epidemic at Camp Travis was accompanied by a large percentage of bronchopneumonia. This complication was brought about by:

1. A lowered resistance due to the toxemia resulting from the influenza infection.

2. By the increased activity of the pneumococcus.

It is the latter organism, in our opinion, which was responsible for the bronchopneumonia and its complications, namely, meningitis and empyema.

Smears and cultures of the sputa of the bronchopneumonias, together with the typing (rats and mice) in the cases showing the pneumococcus, revealed the following:

TABLE II.

Type I	8 cases
Type II	1 "
Type IIa	3 "
Type III	4 "
Type IV	94 "
Pneumococcus, Type unclassified	901 "
Bacillus influenzæ	419 "
Pneumococcus, Type I and influenzæ bacillus	1 "
" " II " " "	1 "
" " IIa " " "	2 "
" " III " " "	2 "
" " IV " " "	2 "
" " II, III " " "	1 "
Streptococcus, unclassified	66 "

The figures above illustrate clearly that the sputa showed the pneumococcus and the Bacillus influenzæ as the organisms most often found, the pneumococcus being of the heterogenous or Type IV variety. This organism is harmless *per se*, but with a lowered resistance of the host it becomes very active and infective.

LUNG PUNCTURES. Lung punctures were made in a number of cases of bronchopneumonia immediately after death. The exudate, which was aspirated, was cultured on defibrinated blood-agar, inulin, and other media. These all showed the pneumococcus.

BLOOD CULTURES. Blood cultures in cases of influenza were all negative. The results in the bronchopneumonias are given in Table III.

TABLE III.

Total number of blood cultures of bronchopneumonia cases	178
Number of cultures positive for the pneumococcus	21
Percentage of positives	11

This 11 per cent. of positive blood cultures is another confirmation of the previous statement that the pneumococcus was the etiological factor in the bronchopneumonias. We were not content with smears alone in arriving at conclusions, but subcultured the organisms recovered from the blood on defibrinated blood agar and inulin cultures and also tested them for bile solubility.

URINE EXAMINATIONS. Of 2000 urine examinations of cases of bronchopneumonia, 385 specimens showed an albuminuria. Granular, hyaline and epithelial casts were found microscopically. Of the 385 having a positive albumin 53 died. These results coincide

with the findings at postmortem, when acute parenchymatous changes were invariably found in the kidneys.

BLOOD EXAMINATIONS. The blood picture of the average case of influenza showed a slight leukopenia, with a relative increase of the small mononuclear cells. Just as soon as bronchopneumonia developed an increase of the polymorphonuclears in the differential counts and a slight increase in the total leukocyte counts were noted. Tables IV and V illustrate the blood findings.

TABLE IV.—DIFFERENTIAL LEUKOCYTE COUNTS, 222 CASES.

Per cent.	1–5	5–10	10–15	15–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90
Polynuclear	..	..	...	...	...	...	3	33	60	76	50
Small mononuclear	..	..	35	38	81	45	21	2			
Large mononuclear	123	19	1								
Transitional	96	2									
Eosinophiles	29	2									
Basophiles	12										

TABLE V.—TOTAL LEUKOCYTE COUNTS, 1084 CASES.

No. of leukocytes per cubic millimeter.	2000 to 3000	3000 to 4000	4000 to 5000	5000 to 6000	6000 to 7000	7000 to 10,000	Over 10,000
Times	32	73	133	163	173	215	295

BLOOD CHEMISTRY IN BRONCHOPNEUMONIA. The results of the chemical examination of the blood in 3 cases of bronchopneumonia are shown in Tables VI, VII and VIII. These cases (J. N., S. K., and J. K.), showed signs of acidosis and were being treated with dextrose solution intravenously. Case J. N. died. Cases S. K. and J. K. recovered. It will be noted in going over these tables that there was a marked retention of urea nitrogen and uric acid, especially while the patients were in acidosis, and that these blood constituents were reduced as soon as they began to improve. Case S. K. showed a marked increase of creatinin at a time when he was expected to die. His condition gradually improved and there was a corresponding decrease in the creatinin. The other 2 cases showed no increase in the creatinin at any time.

TABLE VI.—CASE J. N. (DIED).

	Dec. 8, 1918.	Dec. 11, 1918.
Dextrose: per cent.	0.48	0.16
Creatinin: mg. in 100 c.c. of blood	1.85	2.20
Urea nitrogen: mg. in 100 c.c. of blood	28.50	99.00
Urea: mg. in 100 c.c. of blood	60.95	211.86
Uric acid: mg. in 100 c.c. of blood	6.00	8.80
Chlorides: per cent.	0.43	0.47

TABLE VII.—CASE S. K.

	Dec. 1.	Dec. 3.	Dec. 4.	Dec. 5.	Dec. 7.	Dec. 8.	Dec. 9.	Dec. 13.
Chlorides: per cent.	0.44	0.48	0.51	0.52	0.52	0.51	0.47	0.570
Dextrose: per cent.	0.13	0.15	0.14	0.15	0.13	0.11	0.156	0.212
Creatinin: mg. in 100 c.c. of blood	1.00	2.50	2.20	4.00	5.10	5.00	2.70	1.50
Urea nitrogen: mg. in 100 c.c. of blood	20.75	32.25	83.50	114.00	148.00	85.00	61.00	36.000
Urea: mg. in 100 c.c. of blood	44.40	69.01	179.69	243.90	313.10	181.90	134.54	77.000
Uric acid: mg. in 100 c.c. of blood	6.40	7.30	10.00	10.40	11.80	9.60	6.70	5.200

TABLE VIII.—CASE J. K.

	Nov. 4.	Nov. 6.	Nov. 7.	Nov. 8.	Nov. 9.	Nov. 12.
Dextrose: per cent.	0.12	0.10	0.12	0.10	0.12	0.11
Creatinin: mg. in 100 c.c. of blood	2.85	2.14	1.85	1.05	1.10	1.00
Urea nitrogen: mg. in 100 c.c. of blood	26.50	25.00	20.25	17.50	15.30	12.00
Urea: mg. in 100 c.c. of blood	55.71	53.50	43.33	37.45	32.70	25.70
Uric acid: mg. in 100 c.c. of blood	4.30	..	3.05	2.25	1.93	1.21
Chlorides: per cent.	0.56	0.51	0.53	0.52	0.50	0.51

It is our opinion that the marked increase of the blood constituents referred to is due to protein injury, disintegration and autolysis accompanying excessive lung inflammation.

Table IX illustrates cases of pneumonia without any kidney involvement showing a distinct increase of urea nitrogen.

TABLE IX.

Name.	Lung involvement.	Albumin.	Casts.	Urea nitrogen, grams per 100 c.c.
Clausen	Both bases	Negative	Negative	27.25
Werhane	Both bases	Negative	Negative	44.10
Nichols	Left lobe	Negative	Negative	28.50
Fitch	Right base	Negative	Negative	23.70
Lanier	Extensive	Negative	Negative	34.10
Cannon	Left base	Negative	Negative	47.10
Baum	Right base	Negative	Negative	19.50
Alexander	Left base	Negative	Negative	19.50
Burke	Left base	Negative	Negative	19.00

Table X illustrates cases of pneumonia with kidney involvement showing retention of urea nitrogen.

TABLE X.

Name.	Lung involvement.	Albumin.	Casts.	Urea nitrogen, grams per 100 c.c.
Viertel	Both bases	Positive	Granular	21.30
Peters	Both bases	Positive	Negative	27.75
McDonald	Right base	Positive	Granular	16.30
Powlouski	Left lung	Positive	Granular and hyaline	41.10
Notzelman	Left lung	Positive	Granular	29.50
Helmbrecht	Right base	Positive	Negative	16.20
Florez	Both bases	Positive	Granular	32.00
Donnelly	Left lung	Positive	Granular and hyaline	53.00
Brown	Left base	Positive	Granular	31.20
Brememour	Left base	Positive	Granular and hyaline	26.00

In comparing Tables IX and X the conclusion of the writer is that the retention of urea nitrogen is due principally to protein

disintegration and autolysis associated with the pneumonic process, and that kidney involvement of a transient nature complicating pneumonia has no additional effect on the urea nitrogen content of the blood.

ACIDOSIS. Many of the cases of influenza pneumonia showed evidence of acidosis. This condition was demonstrated by a reduced combining power of the blood plasma for carbon dioxide. In these cases intravenous injections of 10 per cent. to 25 per cent. dextrose solution produced excellent results by acting as a food, producing diuresis and by helping to rid the tissues of the accumulated carbon dioxide. Table XI illustrates the figures obtained in cases of influenza pneumonia with the Van Slyke apparatus.

TABLE XI.

Name.	Lung involvement.	Kidneys.	CO_2 combining power blood plasma, per cent.
Viertel	Both bases	Nephritis	46
McDonald	Right base	Nephritis	54
Fitch	Right base	Normal	51
Notzelman	Left lung	Nephritis	44
Helmbrecht	Right base	Nephritis	63
Florez	Both bases	Nephritis	45
Brown	Left base	Nephritis	47
Hokanson	Right base	Nephritis	48

PLEURISY AND EMPYEMA. It is striking that out of over 2000 bronchopneumonias there were, all told, but 49 cases of pleurisy or empyema. Table XII shows that 25 of the fluids gave positive smears or cultures. Those that were positive showed the pneumococcus present 16 times.

TABLE XII.

Pneumococcus unclassified	11 cases
Pneumococcus and streptococcus	1 "
Pneumococcus and influenza bacillus	4 "
Influenza bacillus	1 "
Pneumococcus, Type IV	2 "
Pneumococcus, Type I and streptococcus	1 "
Pneumococcus, B. influenzæ, B. friedländer	1 "
Friedländer bacillus	1 "
Streptococcus hemolyticus	1 "
Streptococcus unclassified	2 "
Total	25 "
Cases with negative cultures	24 "
Total	49 "

The chemical examination of the blood was done in a number of empyema cases and the findings are seen in Table XIII. Most of them show an increase of the urea nitrogen content of the blood.

TABLE XIII.

Case.	Mgm. per 100 c.c. of blood.				Per cent.	
	Creatinin.	Urea.	Urea nitrogen.	Uric acid.	Chlorides.	Sugar.
H. H.	1.10	31.56	14.75	..	0.64	0.14
J. M. C.	2.00	28.89	13.50	1.40	0.66	
S. M.	2.70	36.97	17.25	4.10	0.65	0.08
W. B.	1.25	41.59	18.50	1.60	0.69	0.13
J. M.	1.26	29.42	13.75	1.50	0.65	0.10
E. W.	1.53	32.63	15.25	1.50	0.70	0.12
T. B.	1.75	52.96	24.75	1.25	0.59	0.13
M. M.	1.85	27.82	13.00	3.25	0.68	0.12
W. H. B.	1.10	45.15	21.10	1.50	0.52	0.13
H. T.	0.70	23.54	11.00	0.90	0.51	0.10
S. Z.	1.85	30.96	14.00	1.75	0.56	0.11
W. J.	1.20	32.74	15.30	1.50	0.51	0.09
H. B.	1.00	40.60	19.00	1.42	0.52	0.10
D. C.	1.10	28.89	13.50	5.10	0.56	0.02
T. T.	1.70	30.16	14.00	0.42	0.55	0.08
M. M.	1.85	27.83	13.00	3.25	0.68	0.12

MENINGITIS. The other complication of postinfluenza bronchopneumonia was meningitis. There were 16 cases in all. The pneumococcus was the organism isolated both by smear and culture in every case. The typings of the pneumococci recovered are given in Table XIV.

TABLE XIV.

Pneumococcus unclassified	3 cases
Type I and IIa	2 "
Type II	3 "
Type IIa	1 "
Type IIa and III	1 "
Type IV	6 "
Total	16 cases

GROSS AND MICROSCOPIC AUTOPSY FINDINGS OF POSTINFLUENZA BRONCHOPNEUMONIA. During the epidemic 26 autopsies were performed at this base hospital. A very careful study of the heart, lungs, liver, spleen, and kidneys was made. Following is a summary of the gross and microscopic findings on cases of postinfluenza bronchopneumonia:

Heart. In most of the cases the pericardial sac contained a straw-colored or a greenish-yellow fluid in excess of normal. In a small number of cases there were pleuropericardial adhesions. The heart as a whole was not markedly enlarged. The right auricle and right ventricle in nearly every case showed varying degrees of dilatation, and the left ventricle was almost constantly hypertrophied. The musculature of the left ventricle was generally of good color and tone. In a few cases vegetation or a sclerotic condition involved the mitral valve, and a few cases showed incompetency of the pulmonic semilunar valves and the tricuspid valves.

Pleura. With but one exception pleural adhesions, fresh in character and easily separated, were present, and these were more con-

stantly on the right side than the left, in the apical region. In some cases the surface of the lungs was covered with a greenish-yellow, friable exudate of a "butter-like" appearance, at times attaining a thickness of one-half inch.

Left Lung. Usually both lobes were the sites of patchy areas of consolidation. This condition was more pronounced in the lower lobe than in the upper. Pulmonary edema existed throughout the lobes not affected by consolidation. No fibrinous plugs could be pressed from the incised bronchi. On section, all stages of consolidation were noted.

Right Lung. Without exception the lower lobe of the right lung contained in some part of it if not in its entirety, consolidation so marked that it could not be differentiated from lobar pneumonia. Nearly every case showed some patchy area of consolidation in the middle and upper lobes as well. In a small number of cases the middle lobes were free from such involvement.

Liver. This organ was constantly enlarged, its surface smooth and of a "boiled liver" appearance. The capsule was not abnormally adherent. The organ cut with firm resistance, and blood exuded from the fresh surfaces. In some instances there was a greenish cast to the cut surface, suggesting biliary stasis. The gall-bladder was invariably distended with bile of varying degrees of viscidity.

Spleen. This organ was invariably larger than normal and markedly congested. In a limited number of cases the congestion was so marked that the spleen resembled a large mass of clotted blood.

Kidneys. Most cases found the kidneys to be enlarged and on section showed marked congestion and prominent outstanding of the Malpighian pyramids with widening of the cortex. In one case the left kidney was about one-half normal size, but it, like the others, presented the characteristics of an acute parenchymatous inflammation. As a rule the capsule of the kidney could be easily removed, but in a few instances it was abnormally adherent and the microscopic picture of these organs was that of a chronic interstitial change.

Microscopic Findings. *Lungs.* The lungs showed an infiltration about the terminal bronchioles of mononuclear cells. The alveolar spaces in the immediate vicinity were filled with an exudate of epithelial cells, mononuclear cells, red cells and fluid. Some cases showed this exudate in various stages of its formation and dissolution. One could note in cases in which consolidation was massive, that the lesion was one of confluent pneumonia, as neighboring areas showed different stages of hepatization. At times one saw a thinning and rupture of the alveolar walls adjacent to these areas of consolidation.

Liver. The vascular structure of the liver showed marked engorgement, with almost invariable extravasation of blood around the central veins of the lobules. The liver cells were swollen and cloudy and

in many instances were larger than normal, making the hepatic cell chains stand out prominently in the liver lobules. The sinusoidal spaces were larger than normal. No areas of focal necrosis were noted.

Spleen. Throughout the sections studied there was a condition of cloudy swelling of the parenchymatous structure. The engorgement was pronounced.

Kidneys. The epithelia of the Malpighian tufts and those lining the uriniferous tubules were invariably larger than normal and of a hazy appearance, with nuclei staining weakly and desquamated. Some of the lumina of the tubules were completely occluded by either the swelling or desquamation of the lining epithelia. Some of the desquamated cells had undergone disintegration. No exudate nor adhesions were noted in the capsule of Bowman. The blood-vessels were very much engorged and red cells were found in the Malpighian tufts and between the tubules. The organs from which the capsule stripped with difficulty showed an increase in the interstitial element, indicative of an inflammatory condition of long standing.

SUMMARY. The epidemic of influenza at Camp Travis was characterized by the presence of the Bacillus of Pfeiffer in 39 per cent. out of a total of 868 throat cultures examined.

Blood cultures in the influenza cases were all negative.

Blood cultures in the complicating bronchopneumonias gave 11 per cent. positives. The organism recovered was the pneumococcus.

The blood picture of the average case of influenza showed a slight leukopenia, with a relative increase of the small mononuclears. When the bronchopneumonia developed there followed a slight increase in the total leukocyte count and an increase of the polymorphonuclears.

Chemical examination of the blood showed a retention of urea nitrogen in the pneumonias having no kidney involvement. The retention of urea nitrogen in cases having a transient nephritis was no greater. It is our opinion that this retention in the bronchopneumonia under discussion was due to protein injury and disintegration associated with extensive lung inflammation.

Blood chemistry in the empyema cases showed a retention of urea nitrogen.

Acidosis was a factor in a large number of the bronchopneumonias at this camp, as was evidenced by a reduction of the combining power of blood plasma for CO_2.

REVIEWS.

THE PRINCIPLES OF NURSING. By CHARLOTTE A. BROWN, R.N., Superintendent of Nurses in the New England Hospital for Women and Children; Graduate, City Hospital and Boston Lying-in Hospital Training School for Nurses; late Instructor in the Boston City Hospital Training School for Nurses. Pp. 255. Philadelphia and New York: Lea & Febiger, 1919.

MISS BROWN has written a book on nursing which is likely to be received with considerable enthusiasm by the nursing profession. The text is clear and brief. In fact, this would be the main criticism that one could offer. The brevity and the description in some of the procedures is such that it would be impossible to properly carry out the various steps unless they had been demonstrated before.

J. H. M., JR.

SURGICAL CLINICS OF CHICAGO. Vol. III, No. III. Pp. 287; 118 illustrations. Philadelphia: W. B. Saunders Company, 1919.

THIS number of the *Clinics* is an exceptionally interesting and instructive one. The number and character of the subjects treated make it especially valuable. The list of contributors contains the names of some of the most able men not only in Chicago but in this country.

Several very rare and perplexing conditions have been exploited, and their treatment outlined, such as cysts of the urachus, diverticulum of the esophagus, complete volvulus, stricture of the esophagus, etc. A very interesting article is included on sterility. Injuries of the joints, both in war and civil life, are discussed, as well as the most recent ideas on the surgical treatment of empyema.

The first contribution, on studies in paleopathology, although having but little bearing on present-day surgery, is most interesting from a historical viewpoint. It describes the most ancient of surgical practices—namely, trephining—and abundantly illustrates many specimen skulls, showing the various methods employed by different peoples scattered over the world as far back as the Neolithic times.

E. L. E.

PNEUMOTORAX ARTIFICIAL Y OTRAS INTERVENCIONES EN LA TUBERCULOSIS PULMONAR. Estudio critico y clinico por el DR. JUAN B. MORELLI, Profesor de Clinica Terapeutica de la Facultad de Medicina. Two volumes. Pp. 1247; 60 illustrations and 8 plates. Montevideo: Imprenta Nacional, 1918.

ARTIFICIAL pneumothorax, as a method of treatment for pulmonary tuberculosis, though systematized by Forlanini, in 1882, had been suggested by the English physiologist Carson in the second decade of the nineteenth century on the same grounds as recommended by Forlanini; and even before Carson's time it is known that Baglivi had observed two patients with phthisis who were markedly improved as the result of pneumothorax which followed gunshot wounds. The method, though known and employed in Italy from the time of Forlanini's early work, was scarcely known at all in other countries; in the United States it was independently proposed by John B. Murphy, in 1898, and its adoption on this continent is due largely to his teachings. Morelli was himself the first (1910) to adopt the method in South America.

The tuberculous process comprehends two stages: (1) Infiltration—which stage is curable by hygienic measures, and (2) caseation—which is incurable by hygiene alone, and which in the lung is always attended by surrounding inflammatory changes, leading to progressive destruction, owing to the constant movement of the lungs, this latter factor (constant motion) not being present in other structures such as bones and lymph nodes, which even when affected by tuberculous caseation are susceptible of cure much more readily than is the lung. The alternative methods of cure for this advanced stage of the tuberculous process, according to Forlanini, are *extirpation* of the diseased lung or its *immobilization*. The former method has been abandoned after sufficiently disastrous experiences; but to further popularize the latter method (immobilization) the present treatise has been prepared, based on Morelli's own large personal experience and on a painstaking and comprehensive study of the literature. The bibliography of the subject, assembled at the end of the work, occupies no less than thirty pages.

After the historical introductory chapter, Morelli proceeds to describe the apparatus and technic employed in the induction of artificial pneumothorax by Forlanini, Murphy, Brauer, Saugman and others who have specialized in this field of phthisiotherapy. There follow interesting chapters on the pathological physiology of artificial pneumothorax, including discussions of the mechanics of the pleural vacuum, pressure pneumothorax (open and closed), the composition of gases introduced into the pleura, their rates of absorption and the chemical changes which they undergo. He next discusses in more detail the ends sought to be gained and the

methods of introducing the gas at the first sitting and on subsequent occasions; the importance and interpretation of manometrical observations; the immediate effect on the patient; complicating factors such as adhesions; accidents occurring during the introduction of the gas or during the intervals between treatments; results of treatment; theories as to how pneumothorax produces these results; and finally a few chapters are devoted to other operations for the cure of pulmonary tuberculosis, such as the production of extrapleural pneumothorax, artificial pleural effusion, intrapulmonary injections, extirpation of the diseased portions of the lung, opening and draining of cavities, resection of the costal cartilages, section of the phrenic nerve, extrapleural plombage, etc.

It is impossible to give here more than a very brief summary of a few of the interesting topics treated at great length in this extensive work. The following items have been selected:

Artificial pneumothorax cannot be produced in from 15 to 25 per cent. of cases in which it is indicated, owing to pleural adhesions. In many patients the first injection produces such marked amelioration that too sanguine hopes of rapid and absolute cure are engendered. Usually complete collapse of the lung must be secured and maintained for a long time before any permanent results can be expected; but each patient has his individual optimum limit of collapse, and greater pressure and collapse than this optimum are harmful.

The results may be seen in the following statistics: Brauer and Spengler, in 1910, reported on 114 patients, of whom 26 were not suitable for this treatment, leaving 88 who were treated by artificial pneumothorax; of these 88, 27 (33 per cent.) were absolutely or relatively cured and 36 (40 per cent.) were improved, 6 were not improved and 19 died. T. Sachs (1915) assembled the statistics of North American authors covering 1147 cases, the results being known in 1108; in 15 per cent. treatment was prevented by adhesions, in 18 per cent. no improvement occurred and 16 per cent. died—or a total of 50 per cent. of non-success; 29 per cent. were improved and 21 per cent. were more or less completely cured; but when these apparent cures were traced for months or years it was found that actually only 12.3 per cent. remained finally cured.

Treatment by pneumothorax must be supplemented by hygienic and dietetic (superalimentation) measures. Forlanini thought it had no favorable action in cases of simple early tuberculosis, and reserved it for cases which had progressed to the stage of caseation; but Morelli believes it may be of benefit even in early stages, and suggests that the compression procures some form of serological reaction which proves beneficial. It is the most valuable known remedy against hemoptysis.

The injections are made under local anesthesia; the needle is thrust quickly through the skin and then pushed cautiously onward,

millimeter by millimeter, every two or three seconds, with constant manometric control; the appearance of negative pressure indicates that the pleura has been entered, which is preferably accomplished during an inspiration; respiratory oscillations will then appear in the manometer and the introduction of the gas may be commenced.

Some competent authorities (as Saugman) do not increase the pressure on the first injection above the neutral point between negative and positive pressure, except in cases in which, owing to adhesions, only a partial pneumothorax can be produced, when they permit a pressure +5, but even at subsequent injections they never allow the pressure to exceed +20 to +25. Forlanini, however, uses pressure up to +60 if the heart and mediastinum are not disturbed. The intrapleural pressure always falls gradually but steadily after the injections, in part owing to the evacuation (through the bronchi) of the residual air in the lung, and in part owing to absorption of the gas from the pleura. Forlanini teaches that an average of 100 c.c. daily is absorbed in the days just succeeding the injection; during the first year an average of 1 liter a month is absorbed. Morelli, however, considers these figures very much higher than the truth. In most cases the *intrapleural pressure* falls to 0 in twenty-four hours.

Physical and radiological examinations are necessary to indicate the most favorable site for the first puncture. Forlanini introduced only 300 to 400 c.c. on the first injection, and Morelli thinks better results are obtained by small amounts regularly introduced at short intervals than by larger amounts at irregular intervals. Every second or third day is often enough, but in urgent cases (as to check hemoptysis) the injection may be repeated on the same day. In the most favorable cases complete collapse will be secured in from fifteen to thirty days; but in the majority of cases phenomena of partial collapse of the other lung, of pain from rupture of adhesions on the same side, or other complication, necessitate the abandonment of regular injections before complete collapse can be obtained, and the course of treatment must be prolonged over several months. When collapse has at last been secured (as evidenced by the absence of visible pulmonary movement under fluoroscopic examination) it must be maintained by periodic reintroduction of gas. Usually a neutral pressure is best tolerated; but the presence of a resistant cavity which does not collapse with the rest of the lung, the failure of the patient to improve even when complete collapse is maintained or the presence of adhesions to the parietal pleura require a positive pressure. If occasional expansion of the collapsed lung is allowed to occur the patient invariably shows the bad effects of the change. A. P. C. A.

RECONSTRUCTION THERAPY. By WILLIAM RUSH DUNTON, JR., M.D., Assistant Physician at Sheppard and Enoch Pratt Hospital, Towson, Maryland; Instructor in Psychiatry at the Johns Hopkins University; President of the National Society and of the Maryland Society for the Promotion of Occupational Therapy; Secretary of Maryland Psychiatric Society. Pp. 236; illustrated. Philadelphia and London: W. B. Saunders Company, 1919.

THE subject of occupational therapy and reconstructive therapy is of prime importance at the present time following the war, but it is a phase of medicine which should be carefully studied at all times on account of the frequency of industrial accidents, the large number of blind who are always with us, the feeble-minded and the mentally inefficient. The book is carefully prepared, is extremely suggestive and filled with splendid ideas. It will be of value to all those interested in proper education of those who have been so unfortunate as to be abnormal. J. H. M., JR.

COLLECTED PAPERS OF THE MAYO CLINIC, ROCHESTER, MINN. Edited by MRS. M. H. MELLISH. Vol. X, 1918. Pp. 1196; 442 figures. Philadelphia and London: W. B. Saunders Company, 1919.

THE Mayo Clinic volume for 1918 contains ninety-five papers by forty-six different authors, seven of whom (Balfour, Henderson, Judd, C. H. Mayo, W. J. Mayo, Rosenow and Stokes) have contributed more than five articles apiece. A suggestion made by the present reviewer, on a former occasion, has been adopted, and the list of contributors now contains information of the status of each in the Mayo Clinic and in the Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota.

Papers dealing with the alimentary canal occupy less than a fourth of the volume, those dealing with the head, trunk and extremities an equal space; while the remainder is devoted to the urogenital organs (90 pages), ductless glands (30 pages), heart (20 pages), blood (100 pages), skin and syphilis (120 pages), nerves (20 pages), technic (50 pages), and miscellaneous subjects (125 pages).

Probably the most important of these contributions is a series of papers by W. J. Mayo, dealing with the cirrhoses of the liver. He advocates splenectomy as a method of "relieving the subnormal liver of its overload," and believes the mere mechanical relief secured the liver by shutting off such a large proportion of the blood normally delivered to it may prove beneficial, though he also recognizes the probability that splenectomy also reduces or eliminates a constant stream of infection sent to the liver from the spleen, the latter having strained out from the circulation its infectious con-

tents. In portal cirrhosis he thinks splenectomy should be considered as a means of relieving the overburdened liver; it is a procedure which is much more certain to secure the desired effect than is the attempt to shunt the portal circulation directly into the systemic by means of Talma's operation of epiplopexy with its associated maneuvers intended to create a collateral circulation. Of five patients with portal cirrhosis treated by splenectomy, Mayo says four recovered from the operation and were markedly improved. He suggests, as a further means of relieving the subnormal liver, the ligation and division of the inferior mesenteric or superior rectal artery and vein, a procedure which diverts all the blood from the territory tributary to these vessels from the portal system into the vena cava by way of the middle and inferior rectal veins. Yet the query propounded by Blake when this subject was under discussion by the American Surgical Association, remains unanswered: Does removal of the spleen diminish the *hepatic* circulation?

Portal cirrhosis, Mayo believes, is related to the defense function of the liver, being an attempt to encapsulate and destroy chemical poisons, especially when the spleen has become incompetent. He denies the existence of Hanot's cirrhosis, claiming such cases are either instances of hemolytic icterus or of ordinary "biliary cirrhosis." The former is primarily a disease of the spleen, with secondary work-hypertrophy of the liver, and he notes that in 50 per cent. of his own cases of splenectomy for hemolytic icterus, gall-stones have been present, with recurring attacks of infection.

The subject of biliary cirrhosis, however, is not so clear as is that of portal cirrhosis; apart from the fact of its infectious origin, and that it may exist in acute or chronic form, little is definitely known about it. Moreover, there is the disease known by Concato's name (1881) called polyserositis, and its subvariety, known as Pick's syndrome, in which the predominating symptoms are caused by the pericardial lesions. Between these affections and tuberculous peritonitis, and tuberculous effusions in the pleura and pericardium, the boundary line is not always clear.

Plummer has an interesting article on the blood picture in exophthalmic goitre; his conclusions are that lymphocytosis (average about 35 per cent.) is characteristic and therefore of value in diagnosis; and that leukopenia if present occurs at the expense of the polynuclears; yet that the blood picture is of no value in prognosis nor in determining the degree of severity of the disease. Pemberton's paper on blood transfusion gives an admirable historical summary, and contains records of more than 1000 transfusions by the citrate method, which he prefers to all others.

In view of the previous statistics and pathological studies published from the Mayo Clinic, it is interesting to note that Judd acknowledges (p. 204) that it seems probable that most gastric cancers begin as cancers—not as ulcers.

A. H. Logan contributes a good paper on chronic ulcerative colitis, illustrated with a remarkable series of skiagraphs.

It is surprising to read W. J. Mayo's expressions of admiration for the fact that in St. Mark's Hospital, London, *fistula in ano* and hemorrhoids have been well treated for more than forty years, and especially that he describes the operations for these affections as if unknown to fame. Attention is called to the matter by the reviewer for the same purpose that it is mentioned by Mayo—to promulgate the proper methods of operation if they are unknown.

Although all the papers in these annual volumes from the Mayo Clinic are published elsewhere in periodical literature, their preservation in collected form has become indispensable to the active surgeon; and the publishers and editor, no less than the various contributors, may feel that they continue to deserve well at the hands of the profession. A. P. C. A.

MALARIA AND ITS TREATMENT IN THE LINE AND AT THE BASE. By CAPTAIN A. CECIL ALPORT, R.A.M.C. (T.), M.B., CH.B., Edin., late Acting Major, Officer-in-Charge of the Medical Division of the Twenty-eighth General Hospital and of the Forty-first General Hospital, Salonika. Pp. 279. New York: William Wood & Co., 1919.

THE treatment of malaria is an extremely important phase of military medicine, particularly so among troops in the subtropical regions. Dr. Alport had a very extensive experience in the Balkans, and the results of this experience are embodied in the present volume. Much credit is due the author on account of the difficulties of doing literary and careful clinical work under the stress of active campaign. As he was far distant from reference libraries, the book is entirely a record of personal opinion and of personal results. For that reason it is of considerable value.

Dr. Alport advises the bihydrochloride salt of quinin, largely on account of its extreme solubility. Quinin is given by mouth, by intramuscular and by intravenous injection.

The author prefers giving quinin by intravenous transfusion, because, as he says, it is the most scientific and the most efficacious method of administration. It is as safe as any other method, and is not disagreeable. The quinin is given in amounts varying from 20 to 40 grains dissolved in 8 ounces of normal salt solution. There is danger of too great concentration of the quinin. At least 8 ounces of saline solution is the minimum amount that has proved correct and safe in the author's studies. Of course, it is not necessary to give quinin this way except in severe types of malaria.

In regard to the administration of quinin by mouth, it is recommended that it never be given in tablet form but given either as a powder or in solution, preferably solution, when possible. The intramuscular injections are not always pleasant nor entirely free from the danger of local nerve palsies.

Criticism of the author's methods of treatment are not exactly just if one considers the place and difficulties under which he worked. In mild cases of malaria he seems to give quite small doses of quinin over too long periods of time, and it is quite possible that the parasites in some of these patients become quinin-fast, a possibility which is apparently not recognized by the author. The outstanding criticism of the book itself is that it is too full of case histories to make easy or attractive reading, and it has too many illustrations of patients, some up and about, others in bed. Reference to the legend is necessary, in order to see if these soldiers are sick, recovering or entirely well. J. H. M., Jr.

Trench Fever. By Major W. Byam, R.A.M.C., Captains J. H. Carroll, U.S.R., J. H. Churchill, R.A.M.C., Lyn Dimond, R.A.M.C., V. E. Sorapure, R.A.M.C., R. M. Wilson, R.A.M.C., and L. Lloyd, R.A.M.C. With an introduction by Lieut.-General Sir T. H. Goodwin, K.C.B. Pp. 196; 48 charts and diagrams. London: Oxford University Press, 1919.

This book is an account of the Trench Fever Commission's work at Hampstead. They have definitely proved that trench fever is transmitted by the body louse; the head and body louse are the two varieties capable of this transmission. It is the excreta of the louse which is the damaging feature. In all probability the organism causing the disease undergoes some cycle or development within the louse, as they have been unable to cause the disease before five days after the louse has fed upon an infected individual. The infective power of the louse has been proved to be at least twenty-three days. The excreta from a single louse has been sufficient to cause trench fever in an adult. Whole blood taken from a vein of a patient is capable of producing the disease in a healthy adult when given into a vein. The plasma alone is not capable in doing this. They call attention to the presence of Rickettsia bodies, but do not believe they are the causative factor. All experiments are recorded fully, testing out the modes of transmission, virulency of the virus, etc. Experiments were made upon men who volunteered for this purpose. They divide the fever into five different types, giving the symptomatology, pathology, prognosis and treatment of the disease as a whole. They have proved that one attack confirms a certain degree of immunity.

Eighty-five per cent. of the cases treated recovered. The remainder of the chronic cases assumed the same symptomatology as the disordered heart cases, and all feel that trench fever is one of the most important etiological factors in this affection. A chapter is devoted to geographic distribution and another to the prophylaxis of the disease.

In the appendices the experiments are recorded more fully. A summary of the report of the commission of the American Red Cross Research Committee on Trench Fever is also appended. The results of both bodies are practically the same. A great deal of credit should be given these workers, as well as those who volunteered for the experiments, as the knowledge gained is of extreme value to all communities of the world. T. K.

THE NERVOUS HEART: ITS NATURE, CAUSATION, PROGNOSIS AND TREATMENT. By R. M. WILSON, Captain, R.A.M.C., Cardiologist to the Trench Fever Research Committee, and JOHN H. CARROLL, Major, M.C., U.S.A., Instructor in Clinical Medicine, University and Bellevue Hospital Medical College. Pp. 136; 55 illustrations. London: Oxford University Press, 1919.

THIS volume is the result of much research work done at the military hospital at Hampstead and Mount Vernon. The authors have attacked the nervous heart problem from the standpoint of the vagus depressor and sympathetic nervous systems, at all times feeling that an infection or a toxemia is the primary basis for the break in the normal relation between these two nervous systems. The infections are again divided into the acute, such as pneumonia, diphtheria, scarlet fever, etc., in which eventually all evidences of toxemia will disappear with the subsequent recovery of the patient; and into the more chronic such as trench fever, tuberculosis and rheumatism. These cases are, as a rule, the unfavorable cases as to recovery. The symptomatology of the disease, breathlessness, giddiness, precordial pain, pulse-rate and the vasomotor phenomena are all explained from the sympathetic and vagus depressor viewpoint. The treatment is based upon the removal of the infection or toxemia; secondarily, the palliative treatment consists of personal reassurance of freedom of serious cardiac disease, encouragement to return to vocational work in the same environment as formerly, and in addition graduated exercises to stimulate the sympathetic system to respond more freely to the hypersensitive vagus. Thyroid extract and atropin have been the only two drugs of value in these cases.

The work is undoubtedly a step in the right direction toward finding an explanation upon a physiological basis of this condition.

T. K.

TRANSACTIONS OF THE SECTION ON GENITO-URINARY DISEASES OF THE AMERICAN MEDICAL ASSOCIATION. CONTRIBUTED BY TWENTY-ONE MEMBERS. Pp. 260; 30 illustrations. Chicago: American Medical Association.

A VOLUME well in keeping with its splendid predecessors, containing seventeen essays of the highest character and of great surgical interest. An especially valuable contribution is by J. T. Geraghty on an intimate study of one hundred and forty-five cases of bladder tumor, outlining the close differential diagnosis and giving the technic of treatment by fulguration and radium and his results. This is followed by B. S. Barringer detailing his technic with radium needles in cancer of the prostate. The symposium on lithiasis, by E. W. Caldwell, L. T. Le Wald, E. L. Young and H. G. Bugbee, is a second valuable study in diagnosis and treatment. The paper by F. W. Robbins and F. P. Seabury on their new method of treating chancroid, which has so revolutionized the treatment of these cases, should be studied and followed to appreciate its full importance.

A. R.

A MANUAL OF EXERCISES FOR THE CORRECTION OF SPEECH DISORDERS. By MAY KIRK SCRIPTURE, B.A., Instructor in Speech, Columbia University; Director of Speech Correction, Vanderbilt, etc., and EUGENE JACKSON, B.A., in Charge of Speech Correction at the University of Bellevue Hospital Medical College Clinic, New York City, etc. Pp. 136; 46 illustrations. Philadelphia: F. A. Davis Company, 1919.

THIS book is really the second volume of two small manuals devoted to the subject of speech defects. The first volume deals with the defects themselves, their etiology, diagnosis and therapy. The second volume, which is this manual, is simply an exercise book for both teacher and pupil. In this work there is no attempt to correlate the various exercises with any specific speech disorder, but it is simply a well-written, properly illustrated series of exercises intended to establish a normal speaking ability. There is an introduction in which various breathing exercises, mouth gymnastics, suggestions for teacher and necessary teaching implements, etc., are described. The rest of the book consists of fifty daily lessons arranged progressively, covering the various procedures and exercises which in the opinion of the authors are the best aids to proper voice control and speaking ability.

This manual should be used in connection with Volume I of this series, and the two make good text-books for the use of those who are devoting themselves to the correction of speech disorders.

G. B. W.

PROGRESS
OF
MEDICAL SCIENCE

THERAPEUTICS

UNDER THE CHARGE OF
SAMUEL W. LAMBERT, M.D.,
NEW YORK,
AND
CHARLES C. LIEB, M.D.,
ASSISTANT PROFESSOR OF PHARMACOLOGY, COLUMBIA UNIVERSITY.

The Effects of Influenza on Pulmonary Tuberculosis.—Although the number of cases observed by STIVELMAN (*New York Med. Jour.*, July 5, 1919, p. 20) were too few for definite conclusions, he calls attention to the following instructive facts: (1) The influenza epidemic appeared at the sanatorium several weeks later than in New York City (which is forty miles south) and only forty-eight hours later than in the nearest village, a half-mile from the institution. (2) Tuberculous and non-tuberculous subjects appeared to be equally susceptible to the infection, the incidence in both cases being 24 per cent. (3) Early and advanced cases of tuberculosis were equally affected. (4) Pneumonic consolidations occurred as frequently in the non-tuberculous as in the tuberculous. (5) The mortality of the epidemic was 11.4 per cent. (6) Careful observation for four months and re-examination of all patients so affected at the end of this period showed that all the patients but two were none the worse for their experience, their general condition being as good as might have been expected normally. (7) So far there seems to be no increase in the number of tuberculous patients seeking admission to the sanatorium as a result of influenza, and more cases are erroneously sent to us for treatment on account of basal lesions than in corresponding periods of the past two years.

The Effects of a Scorbutic Diet on the Adrenal Glands.—MCCARRISON (*British Med. Jour.*, August 16, 1919, p. 200) found that the weight of the adrenals of guinea-pigs dying in consequence of the scorbutic diet (crushed oats and autoclaved milk) is approximately double that of health; this increase is even more marked when the weight of the glands is calculated per kilo of original and of final body weight. The

histopathological changes are hemorrhagic infiltration and disintegration of the cellular elements of the cortex and medulla. These changes are to be regarded as pre-scorbutic in character, as they may occur in animals which exhibit no clinical evidence of scurvy during life. In spite of the greatly increased weight of the adrenal, the total quantity of adrenalin in the two glands is less than half that present in healthy guinea-pigs, while the total adrenalin per gram of gland is less than one-fourth of the normal. In healthy pigeons the total adrenalin per gram of gland is approximately ten times greater than in normal guinea-pigs. In pigeons deprived of accessory food factors there is a great increase in the adrenalin content of the adrenals; the actual adrenalin content is largely dependent on the class of accessory food factor absent from the dietary. When, for example, material containing accessory food factors of class "A" is added to a diet of autoclaved rice the adrenals usually show a normal amount of adrenalin. It appears that lack of factors of the "A" class with excessive production of adrenalin is associated with the occurrence of edema in aves, and that in guinea-pigs lack of factors of the "C" class, with diminished production of adrenalin, is associated with hemorrhage into the body tissues.

Liquid Paraffin for Disinfecting Needles and Syringes. — WATERHOUSE (*British Med. Jour.*, August 2, 1919, p. 136) recommends the use of liquid paraffin, which boils at 360° C., for disinfecting needles, syringes, etc. A simple method is to heat the upper part of a test-tube three-quarters full of liquid paraffin until currents appear (about 150° C.) or rather longer, draw the heated fluid at once into the syringe until it comes into contact with the whole of its interior and then eject it. Caution is needed in heating the paraffin or it may spurt. The advantages of this method are the rapidity and simplicity with which complete sterilization can be effected at the bedside and the absence of deleterious effect upon the needle, which never rusts and remains patent and useful as long as it can be kept sufficiently sharp. The method is particularly useful for needles and syringes for giving intramuscular injections of mercurial cream.

Dakin's Solution.—In the *British Med. Jour.*, May 17, 1919, p. 611, ATTWATER gives the following simplified method of preparing Dakin's solution. Dr. Dakin himself has expressed his approval of the modification advocated. The quantities required for about 10 liters of solution are: chlorinated lime, about 156 gm.; sodium carbonate (anhydrous), half above quantity; sodium bicarbonate, five-twelfths the above quantity. The exact quantities used are immaterial provided they are used in proportion 12 to 6 to 5. The chlorinated lime is dissolved in 5 liters of water, stirred frequently and allowed to stand for from six to twelve hours. 10 c.c. of this solution, 20 c.c. of 10 per cent. potassium iodide solution and 2 c.c. of strong CH_3COOH are then taken and the whole titrated against a decinormal solution of $Na_2S_2O_3.5H_2O$. If the burette reading is r c.c. the remaining two ingredients are dissolved in $\frac{7r-90}{18}$ liters of water, then mixed with the initial solution and allowed to stand for one hour. The supernatent liquid is siphoned off and filtered; the filtered product is Dakin's fluid of the required

strength, showing no trace of free alkali. The advantages of this method are: (1) the time of preparation is reduced by one-half; (2) no sensitive chemical balance is necessary (except when the preparation of the standard solutions for testing is also undertaken; (3) instead of preparing a separate sample of CaO(Cl)Cl to ascertain the percentage of active chlorin the liquid in bulk is itself tested; this is not only quicker but eliminates the chance of errors; (4) the necessity of powdering the chlorinated lime before taking representative samples is obviated.

Dose and Methods of Administration of Diphtheria Antitoxin.—SEARS (*Albany Med. Ann.*, July, 1919), following the rule of Schick, states that 100 units of diphtheria antitoxin should be given for each kilogram of weight. Thus, 1000 units should be given to a child weighing 22 pounds; 2000 units to a child weighing twice as much; and for a normal adult weighing 132 pounds, 6000 units is the correct amount. For purposes of immunization, one-half the therapeutic dose is sufficient. Before giving the serum it is advisable to test the patient's sensitivity to horse serum, either by giving a very small dose (0.1 c.c.), and repeating in twenty minutes with twice the amount and then gradually increasing the dose, or the Schick technique may be used to inject a minute quantity of the serum intradermally. In mild cases of diphtheria, Sears advises the subcutaneous method of administration, or, if rapid absorption is desired, the serum may be injected intramuscularly. In fulminating cases the serum should be given intravenously.

An Investigation of the End-result in One Hundred and Twenty-four Cases of Blood Transfusion.—The following is a brief *résumé* of the results obtained by WAUGH (*British Med. Jour.*, July 12, 1919, p. 39) in a series of blood transfusions carried out in a base hospital in France between November, 1916 and October, 1918. The method employed was indirect transfusion by Vincent's paraffin-coated tubes. The amount transfused was usually 600 c.c. Compatibility was established first by direct comparison of the bloods under the microscope, later by obtaining Group IV donors by the convenient macroscopic method introduced by Lee. The main indications for the employment of transfusion were (Class I) severe secondary hemorrhage; (Class II) preliminary to high amputation of thigh or arm; (Class III) certain cases of pyemia. Class I. (*a*) Secondary hemorrhage; ligation of main artery; (*b*) secondary hemorrhage; amputation of limb. (*a*) Transfused, 52; death-rate, 32.7 per cent.; not transfused, 52; death-rate, 46.1 per cent.; (*b*) transfused, 14; death-rate, 28.5 per cent.; not transfused, 14; death-rate, 50 per cent. Class II. Sepsis or gangrene; amputation of limb. Transfused, 39; death-rate, 10.2 per cent.; not transfused, 29; death-rate, 31 per cent. Class III. Pyemia. Transfused, 19; death-rate, 36.8 per cent.; not transfused, none. Totals, transfused, 124; death-rate, 25.8 per cent.; not transfused, 95; death-rate 42.2 per cent.

The Cure of Multiple Warts on the Face.—IND (*British Med. Jour.*, July 5, 1919, p. 11) recommends the following treatment for the cure of small, multiple warts on the face: The warts and the skin around were painted three times a day for one day with a saturated alcoholic solution of salicylic acid. On the following morning the warts were cut off by a

flat, sharp steel instrument, bevelled on one side only; this passes freely over the healthy skin, but cuts off the warts, leaving only slightly bleeding-points. The surface is then painted with the salicylic solution and twice more during the same day, three times in all. This turns the little red points to a brownish-black color, tiny scabs form which are allowed to drop off, taking about a week to do so, and leaving a perfectly clear healthy skin. The skin is bathed with pure alcohol once a day until the scabs have all dropped off. With this treatment there is neither pain nor scarring, sepsis does not occur and there is no recurrence of the multiple growths.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D., OF PHILADELPHIA.

Fat Metabolism of Infants and Children.—HOLT, COURTNEY and FALES (*Am. Jour. Dis. Children*, September, 1919) continue their observations on the fat metabolism of infants and children. This article concerns the digestion of vegetable fats by children on a mixed diet. They found that the stools of children receiving a considerable proportion of vegetable fat did not differ essentially in appearance from those of children receiving mainly milk fat, although they were usually somewhat softer. The fat percentage of dried weight of the stools averaged somewhat lower when nut butter was taken, and somewhat higher when corn oil was taken, than when the fat in the diet was mainly milk fat. When larger quantities of corn oil were added to the diet the average was much higher. The soap percentage of total fat in the stools was usually a little lower and the neutral fat a little higher with vegetable fat than when the fat of the diet was mainly milk fat. When nut butter was taken the fat excretion in the alkaline stools was lower and in the acid stools it was higher, than when the diet did not contain vegetable fat. When corn oil was taken in considerable amounts the fat excretion in the stools was higher than when the fat of the diet was mainly milk fat. The total fat intake when corn oil was included in the diet was very large and the actual retention of fat always much higher than the normal average for a mixed diet. When vegetable fat formed a considerable part of the total fat intake, the percentage of the fat intake retained was usually higher than the normal average. In a few instances when the stools were acid and in a few when large amounts of corn oil were taken, the percentage retained was low. Individual children observed for considerable periods with changes in the kind and amount of fat intake showed quite as good digestion of vegetable fat as of corresponding amounts of milk fat and no unfavorable effect on general health and nutrition was observed. No children were kept long enough on a diet presumably deficient in fat-soluble A or fat-soluble vitamin to warrant any conclusions as to the effect of such a diet upon growth

and health. One child who was on a diet in which there was no definite source of fat-soluble vitamin, 95 per cent. of the diet being corn oil, ceased to gain in weight on this diet for a period of five weeks, but showed no loss in weight and the general health was unimpaired. Six children, 80 to 95 per cent. of whose fat intake was vegetable fat showed lowered vitality, two developing styes and two others eczema upon the face, which disappeared when the diet was changed to include milk fat. Corn oil and nut butter are valuable foods for children, and are exceedingly well borne and are apparently digested and absorbed with ease. These articles may be safely introduced into the regular diet of children, and then to a considerable degree may be substituted for the more expensive milk fat, given either as milk or butter, but they should never entirely replace milk fat.

Experimental Hydrocephalus.—DANDY (*Ann. Surg.*, August, 1919) in this article has made a valuable contribution to the extremely scant knowledge of this condition, which often occurs in a most inexplicable manner. His work was done on dogs. He was able to produce hydrocephalus by placing an obstruction in the Aqueduct of Sylvius. Dilatation of the third and both lateral ventricles followed this experiment. When one foramen of Monro was occluded it was followed by a unilateral hydrocephalus. When the choroid of one lateral ventricle was completely removed at the time the foramen of Monro was occluded there was not only no dilatation, but the entire lateral ventricle collapsed. This was the only absolute proof that the cerebrospinal fluid was formed from the choroid plexus. At the same time it proved that the ependyma does not secrete cerebrospinal fluid. When the choroid plexus of both lateral ventricles were removed, and an obstruction was placed in the Aqueduct of Sylvius, hydrocephalus still resulted in the third and both lateral ventricles, but at a reduced rate. The fluid formed from the choriod plexus of the third ventricle but could not escape into the subarachnoid space. He showed that cerebrospinal fluid forms in all the cerebral ventricles, and that it is absorbed almost entirely in the subarachnoid space. The sole communication between the ventricular system and subarachnoid space is through the foramina of Luschke and the median foramen of Magendie. The phenolsulphonephthalein test will prove conclusively whether the foramina of Luschke and Magendie or open or closed. Closure of these foramina invariably cause hydrocephalus. Hydrocephalus followed ligation of the Vena Magna Galeni when the ligature was placed at the origin of this vein. Ligature beyond or in the sinus rectus had no effect because there is sufficient collateral venous circulation. The communicating type of hydrocephalus was produced in dogs by a perimesencephalic band of gauze, saturated in an irritant which produced adhesions. This obstruction prevents cerebrospinal fluid from reaching the cerebral subarachnoid space, where most of the cerebrospinal fluid is absorbed. The resultant diminished aborption of fluid results in hydrocephalus. Hydrocephalus followed ligation of the great vein of Galen because of an overproduction of cerebrospinal fluid. In other types of hydrocephalus, both obstructive and communicating, the accumulation of fluid is due to a diminished absorption of cerebrospinal fluid.

Backward, Nervous and Delicate Children.—McCready (*Pennsylvania State Med. Jour.*, September, 1919) calls attention to the fact that many of the causes of nervous and mental deviation, with their constitutional basis are controllable if the manifestations are recognized early enough. He says that constitutional inferiority or hypoplasia may be due to causes which are hereditary or acquired or a combination of both. Hereditary hypoplasia is due to defects in the chromosones of the ovum or spermatozoön of the parents. Environmental hypoplasia is due to toxemia in the parent or parents affecting the ovum or the spermatozoön or both. It may be due to toxemia in the mother or to local disease in the endometrium. It may also be due to bad environment in postnatal life. The child at birth may give evidence of insufficient vital energy such as underdevelopment and asthenia. Asphyxia, especially when followed by convulsions, should require careful investigation for evidence of intracranial pressure. Convulsions during infancy and early childhood usually indicate an unstable nervous system. Chorea is likewise a matter of greater importance than is commonly supposed. Difficulty in feeding, acidosis, enuresis, underweight and the visceroptotic habit, overweight with pudgy extremities and phlegmatic temperament are conditions that demand more consideration than are usually given to them. From a psychic standpoint extreme timidity or its opposite—undue aggressiveness, night terrors, excessive imagination, phobias, compulsive ideas, pathological lying, and extreme egoism call for investigation and correction. Premature eroticism resulting in infantile masturbation and childhood perversion of the sex instinct are frequently associated with a neurotic constitution and should be studied carefully for the purpose of determining the best method of treatment. Treatment of these cases should include all measures, medical, hygienic and educational which have for their purpose the stimulation of the correlative forces of growth, the elimination of waste products, the development of the psychomotor and emotional control, and the cultivation of the higher faculties of the mind.

Toxic Properties of Milk.—Ford (*Am. Jour. Dis. of Children*, September, 1919) presents evidence which shows that when milk, previously heated to 80° or 85° C. for from twenty to thirty minutes, is allowed to decompose it contains bacteria and their products which are capable of giving rise to an acute death in small animals such as rabbits and guinea-pigs on subcutaneous inoculation. This is a true intoxication since the bacterial products when freed from bacteria by filtration through Berkefeld filters are always poisonous and bring on fairly definite changes in animals. Milk cultures of Bacterium welchii are also poisonous and this poisonous action is likewise due to a toxic or poisonous principle present in the milk. The fact that the gas bacillus is the predominant organism in heated market milk and the similarity of action on animals of the heated milk and the milk culture of the gas bacillus make it a reasonable conclusion that the poisonous quality of the decomposed milk is to be attributed to the development in it of this species which is always present in the spore form. The fact that the point of heat destruction of the milk toxin is somewhat higher than that of the gas bacillus toxin may be explained on the assumption that the

market milk may contain other substances than those produced by the gas bacillus, either protein decomposition products or the secretory products of other bacteria, either aërobic or anaërobic in character. It should be said that the toxic substance present in milk cultures of Bacterium welchii is also at times thermostabile and may resist a temperature of 70° to 80° C. The exact relation of the toxic substance formed in milk cultures of this species to the toxic substance recently described by Bull and Pritchett, and shown by them to act as an antigen is not clear. Filtrates from the milk cultures are powerfully hemolytic, and some of their poisonous action may be due to blood destruction. The pathologic picture is not that of a pure hemolytic intoxication, as evidenced by the lack of hemoglobinuria and in many instances the animals die acutely without signs of local blood destruction. It is possible that there are two distinct substances in the milk cultures: one hemolytic and present in considerable quantity and destroyed at about 60° C., in thirty minutes, and one toxic, usually resisting a temperature of 60° C., but produced irregularly. The latter is probably identical with the gas bacillus investigated so carefully by Bull and Pritchett. The demonstrations of these materials in heated milk should be kept clearly in mind in the consideration of the problem of milk pasteurization. Under all circumstances milk heated to temperatures sufficient to destroy vegetative bacteria but not their spores should be kept at a low temperature to prevent the development of these spores and should be used within a short time after the heating. Whether the bacterial products found in this decomposed milk have any poisonous action when taken into the digestive tract has not been determined, but in view of their presence in milk the practice of keeping pasteurized milk for any considerable period of time should be avoided. The occurrence of toxic substances in heated milk arising from the development of spore-bearing bacteria requires a rigid supervision of milk production before pasteurization to prevent the entrance of organisms of this kind.

Cerebrospinal Involvement in Hereditary Syphilis.—JEANS (*Am. Jour. Dis. of Children*, September, 1919) gives the results of the routine observations on all children with syphilis coming to the Washington University Dispensary. Seventy-eight children under two years of age and 136 over two years of age were studied in regard to nervous system involvement. Besides being studied neurologically fundus examination of the eyes were made. The chief purpose of the study was to show the frequency with which the central nervous system is seriously involved in hereditary syphilis. It is usually conceded that if the cerebrospinal fluid gives a positive reaction to the Wassermann test, there is involvement of the central nervous system. The findings of increased cells, globulin, albumin and a positive colloidal gold test though important has not the same significance as the positive Wassermann. Of the 78 infants the serum of all but 1 gave a strongly positive Wassermann reaction. The exception was an infant, one month old, who had a rash, rhinitis and infiltration of the palms and soles. The cerebrospinal fluid of 31 of these infants gave a positive Wassermann reaction. Of these 11 were four plus, 1 was three plus, 10 were two plus and 9 were one plus. Of the 9 one plus reactions 8 were in infants under three months of age, which might be too early for the Wassermann reaction

to be strongly manifest even though the nervous system might be definitely involved. In 6 of these 9 instances the cerebrospinal fluid gave other evidence corroborating the positive reaction. Three were not otherwise examined, but in 1 a later specimen of cerebrospinal fluid gave a four plus Wassermann. Eleven of the 31 infants whose cerebrospinal fluid gave positive Wassermann reactions had clinical signs of neurosyphilis. The signs manifested were chiefly those of meningeal involvement with evidence of deeper involvement in 3. Three patients with convulsions were seen at the ages of three years, three and ten months respectively, soon after the onset of the convulsions. One patient with neck rigidity and other signs of meningitis, but without convulsions, was seen soon after the onset at the age of seven months. Four patients with moderate grades of hydrocephalus were seen at the ages of five and one-half, six, nine and eleven months respectively. Two patients with optic neuritis were seen at the ages of one and one-half and three months, respectively. One patient with hemiplegia and hydrocephalus was seen at the age of eighteen months. Of the 136 children from two to fourteen years of age, 70 have been classed as having a clinically active infection, and 66 as having a latent infection. All but one gave a positive Wassermann reaction in the serum. The exception was a child who had an acute dementing process and whose cerebrospinal fluid gave complete fixation. The children classed as having a latent infection were for the most part brothers and sisters of children having clinically active syphilis. Some of the children having latent syphilis had scars or similar signs of former lesions, but most of them had no signs or symptoms whatever except a positive Wassermann reaction. Of the 70 actively syphilitic 22, or 31 per cent., had a positive cerebrospinal fluid Wassermann. Of the 66 latent cases 13, or 20 per cent., had positive cerebrospinal fluid Wassermann reactions. Of the total 136 older children 35, or 25.8 per cent., had positive cerebrospinal fluid Wassermanns. Of these, 25 had symptoms or signs referable to the central nervous system. In addition to the 22 patients with active syphilis these 25 include 3 with fixed pupils who had no other signs of activity than a positive Wassermann reaction and who were therefore classed as latent. Of these 25 having clinical signs of neurosyphilis 12 had gross mental defect. The more superficial or meningeal symptoms occurred as follows: 2 had acute meningitis with convulsions at three and four and one-half years respectively; 1 had meningitis without convulsions at four years of age; 5 had chronic convulsions which were classed as epilepsy; 2 had arrested hydrocephalus. The submeningeal manifestations occurred as follows: 6 had hemiplegia; 1 had spastic quadriplegia; and 1 had spastic paraplegia; optic atrophy was seen five times, twice with associated lesions; fixed pupils without optic atrophy were seen four times; 1 patient had an acute dementing process; 1 had juvenile paresis and 2 others had sensory changes with the cerebrospinal fluid reactions of paresis. Two of these latter had optic atrophy. The nervous system was involved in 40 per cent. of syphilitic infants, 31 per cent. of older children having active infection and 20 per cent. latent infection. Of the entire group of 214 infants and children the nervous system was involved in 70, or 32.7 per cent. Of those having positive cerebrospinal fluids slightly more than one-third of the infants and slightly more than two-thirds of the older children had clinical manifestations of neurosyphilis at the time of observation.

OBSTETRICS

UNDER THE CHARGE OF

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Labor Complicated by the Funnel-pelvis.—WILLIAMSON (*Am. Jour. Obst.*, October, 1918) reports 106 cases of funnel-pelvis. This was 7.7 per cent. of the number of women examined. Most of these patients were white and the greater number were delivered in the service of the Manhattan Maternity Dispensary New York. The pelvis was considered to be of the funnel type when the transverse diameter of the outlet was 8 cm. or less. Normally this diameter is 11 cm. These patients were first measured in the routine way and then the transverse diameter was measured as follows: A Budin pelvimeter was held by a nurse, the tips were crossed and grasped between the thumbs and index fingers and forced gently, but firmly between the tuber ischii. This measure was taken as the transverse diameter. In all cases having 8 cm. or less, the posterior sagittal diameter was measured. This was done by placing the patient in the lithotomy position, drawing her down upon the table so that it was possible to measure over the sacrococcygeal joint and to midway between the tuber ischii. From this reading 1 cm. was deducted for the thickness of the sacrum and soft tissues. The pubic arch was palpated by the Sellheim method. The cases were divided into absolutely contracted, with transverse diameter 5.5 cm. or under and the relatively contracted between 5.5 cm. and 8 cm. The pelves were divided into three classes: one in which the transverse diameter was from 7.75 cm. to 8; the next between 7 cm. and 7.5 cm. and the third where the transverse diameter was below 7 cm. In 106 cases delivered there were 95 typical funnel type pelves; 10 generally contracted and one flat funnel. Various authors have given measurements under which spontaneous delivery is not likely. Among these patients 65 were delivered spontaneously and 41, or 38 per cent., were delivered by some operation. Most of the operative cases were forceps deliveries. Cesarean section was performed four times. Pubiotomy twice for generally contracted funnel pelvis. In the first of these there was breech presentation and pubiotomy was necessary to free the aftercoming head. Both these mothers made good recoveries. One child died after delivery. Labor was induced in 3 cases and in 1 of these a Cesarean section was done after the abduction. In choosing the time and method of delivery it is not a question as to whether the patient has a contracted outlet of the pelvis, but what the actual conditions present are as developed during labor. So far as spontaneous labor was concerned $7\frac{1}{2}$ cm. transverse with 7.5 cm. posterior sagittal diameter would usually permit the birth of a living child spontaneously. In these cases there was a high percentage of perineal lacerations, 53 per cent.; there were three lacerations extending into the rectum and on 3 cases symphyseotomy was performed. One mother died; 12 infants died or were stillborn; 4 where death could be traced in some degree to operation.

It is thought that the measurement of the transverse diameter of the outlet should always form part of the general measurement of the pelvis. It is difficult to tell how important a factor this may be as there is no way of accurately knowing the size and the consistence of the fetal head. In cases of absolute contraction Cesarean section should be performed at or just before term. Where the case is one of moderate contraction labor may be induced in from thirty-seven to thirty-eight weeks. If bougies are used there is a possibility of infection and also of displacing the presenting part and thus interfering with the mechanism of labor. In children born by induced labor at thirty-seven or thirty-eight weeks the fetal heart should be carefully watched for such children are not as vigorous as those at term. Forceps will usually succeed in delivering these cases because there is a considerable rotation at the sacro-iliac joints in the patient placed in the lithotomy position. In delivering the head in these cases traction should be made downward even at the expense of considerable laceration. If forceps fails section should not be chosen because of the danger of infection. In selected cases pubiotomy may give good results, but the danger of infection and hemorrhage accompanying this operation must be remembered.

The Result of Induced Abortions as Disclosed by Abdominal Section.—REDER (*Am. Jour. Obst.*, December, 1918) had an opportunity of examining 8 cases of sterilization the result of induced abortions. All of the women were married, in good health and none over thirty-five years of age. In each case the abortion was induced soon after the first period had been missed, generally in the second or third week. A catheter or sound was introduced and sounds usually followed within five days. Before the employment of instruments, hot-water douches; hot foot-baths, mustard applications to the lower abdomen, and in 4 of the cases medicines such as ergot or pennyroyal had been tried without success. Of these 8 women 3 had five abortions in two years; 2 six in two and a half years; 1 nine in three years; 1 eleven in three years and 1 fourteen in five years. None of them was seriously sick. A few remained in bed for several days. No physician was consulted. After a week the discomfort usually had passed and the patients did as they were accustomed. Menstruation, however, was irregular, painful and often profuse for months after. In 5 of the 8 this was permanent, while in the other 3 menstruation became normal; 6 had chronic leucorrhea. All had more or less backache, and each abortion increased the severity of the backache. Apparently the general health had not been impaired nor had the pelvic organs been damaged to any serious extent. These patients subsequently desired children and submitted to gynecological treatment, with the hope of making conception possible. When these women were submitted to abdominal section in 7 out of the 8 the abdominal end of the Fallopian tubes was closed, and this was a positive factor producing sterility. In 5 of the 8 there was bilateral hydrosalpinx. In 2 the hydrosalpinx was unilateral. The opposite tube in the latter cases was collapsed and presented a sacculated appearance, the lumen giving evidence of a number of strictures. In 1 case there was no hydrops of the tube, but the tubes were sacculated and the uterine ends were closed. In each case the tubes were down in Douglas's pouch, usually bound down with adhesions and false membranes. On

the left side the tube was buried under the sigmoid, while on the right it was attached by adhesions to the cecum and the appendix. There were no pathological processes in the ovaries. None was in its normal position. All were prolapsed and adherent to the tube. In several cases the ovary, tube, uterus and rectum were matted together. All of the ovaries gave evidence of cystic degeneration. Some were twice their normal size. In over half the cases there was great thickening of the surface of the ovary and all the ovaries were more or less cystic. In most cases the uterus was backward, fixed by adhesions. In treating these cases conservatism was followed; adhesions were freed and the organs brought as nearly as possible into their normal condition and position. The closed ends of the tubes were opened and the tissues were cuffed back and the tubes explored with a sound. The ovary was fixed as near the opening of the tube as possible, and in some cases the abdominal end of the tube was sutured to the ovary. Cystic material in the ovaries was exsected as much as possible. Two of the patients became pregnant and went to full term within twenty months after the operation. These two had bilateral hydrosalpinx, and resection of both ovaries was necessary. They were the youngest of the series, one twenty-six the other thirty. The remaining six women were operated on within the last four years, but have not yet conceived.

Cesarean Section under Local Anesthesia.—The possibility of performing Cesarean section under local anesthesia is illustrated by BROWN (*Am. Jour. Obst.*, December, 1918) in a multipara suffering from mitral stenosis with asthma. There was marked decompensation. The patient's condition was so grave that she could not be moved from her bed. She was given local anesthesia and an operation was performed with the patient in the sitting posture. After the operation she was given free doses of strophanthus and digitalis and recovered sufficiently to leave the hospital and remain in good health for some time. A severe case of toxemia of pregnancy was relieved by Cesarean section under local anesthesia. Both mother and child recovered. The writer also described the case of a tuberculous woman in whom a bag failed to set up labor. The child was small and there seemed every reason to think spontaneous labor would develop. The bag was expelled through the cervix in seven hours without setting up labor. The child was delivered by abdominal section under local anesthesia. The mother gained weight rapidly after the operation and her general health greatly improved.

Two Cases of Cesarean Section with Denuded Lower Segment.—DORMAN (*Am. Jour. Obst.*, December, 1918) performed Cesarean section on two patients in whom the uterus was retracted from the child. The lower segment was so thin that in extracting the child it was difficult to prevent a laceration into the bladder. In one case the obstruction to labor had been a sharp promontory of the sacrum. In this case there was some difficulty in closing the irregular wound of the uterus and there was moderate bleeding. The patient made a good recovery. In the second case the operation was complicated by omental adhesions. The lower segment was torn during extraction down to the bladder wall and the suturing of the tear was difficult.

Normal Delivery Followed by an Unusual Complication.—STEIN (*Am. Jour. Obst.*, March, 1919) illustrates the uncertainty of obstetric cases by describing the following: The patient, aged thirty-one years, was pregnant for the second time, with a negative history as regards illness. The first child had been born five years previously and its eyes had been infected, requiring treatment for some time. The husband had had gonorrhea several years before his wife's first confinement, but at the time of the confinement he was perfectly well. She had been seen during pregnancy and was always found in good condition. Spontaneous labor developed without examination by anyone and terminated in the birth of a living child. The placenta was expelled in the usual manner and the whole confinement was without incident or complication. Immediately after delivery the patient complained of excruciating pain in the right sacro-iliac region, with a temperature of 101.6°, the next day reaching 104°. The pulse was 140. The patient kept up this temperature and pulse with intermissions for nearly two months. The pain in the sacro-iliac joint was the result of strain of the joint, and strapping gave some relief. An examination of the blood showed the Streptococcus pyogenes and the patient was given antistreptococcic injections for three weeks, as much as 20 to 30 c.c. daily. On the tenth day a swelling appeared at the left knee, which on puncture was found to contain purulent material with the Streptococci pyogenes. When the patient left the hospital she was unable to walk on account of the pain in the sacro-iliac joints, but was permitted to go home, using crutches She finally had a brace, which gave her considerable help. When the final examination was made nothing abnormal could be found. Two weeks later she developed high temperature and pulse and a mass in the right groin. The right thigh became swollen and edematous. A large mass developed above Poupart's ligament, the right thigh was swollen and edematous and on internal examination a large abscess was found, originating apparently in the right sacro-iliac region and pointing toward Poupart's ligament. The abscess was apparently extraperitoneal. Roentgen rays showed abscess in the right pelvic region, but the sacro-iliac ligaments were sound. This abscess was opened and found to contain streptococci and staphylococci, and the abscess was traced to the right sacro-iliac joint. The patient finally made a complete and permanent recovery.

Extraperitoneal Cesarean Section for Contracted Pelvis.—BRODHEAD (*Am. Jour. Obst.*, March, 1919) chose this method of Cesarean delivery in the case of a stout woman of average height, at full term, who had a large child. He describes the case of a patient with marked toxemia, evidenced by albuminuria and casts; blood-pressure 150, but without headache; visual disturbance and epigastric pain. The pelvis was slightly contracted and the head in the second position was just entering the pelvic brim. Fetal heart sounds were strong and regular, the membrane having ruptured two days before admission. The amniotic liquid was clear and without odor. The temperature on admission was 102.5°, the pulse 128. The patient was carefully watched in the hospital for a twenty-four-hour test of labor. During the twenty-four-hour test of labor the patient was carefully watched; the pulse was rapid, the temperature about 101° F., and at 10 P.M. the patient was tired out, and there had been no progress since 10 A.M. After the

twenty-four-hour test of labor, with rapid pulse and elevation of temperature, the patient was exhausted, without progress, excepting full dilatation. Extraperitoneal Cesarean section was performed; the peritoneum was incised and the parietal peritoneum sutured with the uterine peritoneum for about six inches in the form of an ellipse. When the uterus was opened a foul-smelling, green, amniotic liquid escaped. The child was in good condition, was extracted by the breech and the uterus was packed with iodoform gauze. The patient's pulse was 160 after delivery, but the general condition was fair. The child, a male, weighed nine and one-half pounds. The temperature subsided in four or five days and mother and child made, ultimately, a good recovery.

The Treatment of Eclampsia.—EDGAR (*Jour. Am. Med. Assn.*, No. 70, 1918) describes the value of prenatal care in the prevention of eclampsia. He instances 9 cases of the toxemia of pregnancy admitted to the hospital, with blood-pressure ranging from normal to 228 mm.; 5 were primipara and 4 multipara. All had albuminuria in the urine, 4 had casts and 1 had blood. There were gastric disturbances and edema in all. The mothers recovered, delivery having been effected in various ways. There were 10 children, 1 case being twins. The writer believes that the old principles for the treatment of toxemic convulsions are still sound, namely, (1) control the convulsions; (2) elimination of toxins; (3) termination of pregnancy. The writer states that he has come to consider the use of morphin as the most valuable agent. He believes in the conservative treatment, but would not deny the value of operation in selected cases. A single low forceps operation is always permissible and ether is the only anesthetic which should be employed with these patients. All forcible dilatation or prolonged manipulation should be avoided. Hydrostatic bags to induce a shortened labor may be employed in which the obstacles to dilatation are not insurmountable. It is sometimes necessary to complete dilatation of the cervix by the hand to permit delivery by forceps. In the case of a primipara with long, undilated cervix abdominal Cesarean section is indicated. In the present stage of obstetric science it is interesting to observe that the poor are receiving more intelligent treatment than many who are well-to-do.

An Interesting Mole.—BERRI (*Semaine med.*, No. 25, 1918; *Surg., Gynec. and Obst.*, September, 1918) records the case of a patient, aged forty years, with a history of 9 previous pregnancies, 6 ending normally at term and 3 in abortion. The patient gave a 4 plus Wassermann reaction. In the present illness there was amenorrhea for six months and metrorrhagia since the fourth month of pregnancy. When admitted to the hospital the patient was seven months advanced. On coming to the hospital the woman aborted a discharged ovum corresponding in size and aspect to that of a three months' pregnancy. Careful examination of the specimen failed to discover a fetus or any vestiges of one. The embryo had perished in the early months and had been absorbed. The tissue discharged had the characteristics corresponding to the tuberous hematoma described by Breus. The placenta was retained a long time in the uterine cavity and showed structural alterations, due to autolytic processes.

GYNECOLOGY

UNDER THE CHARGE OF

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Injection of Air in Bladder Diagnosis.—The examination of the bladder for tumors by the expert cystoscopist has been so successful that this modified roentgen method has probably not been developed to the fullest extent according to PFAHLER (*Am. Jour. Roentgenology*, 1919, vi, 371), but there are many cases in which an examination by the cystoscopist is not practical because of pain, inability to pass the instrument, hemorrhage or objection on the part of the patient. The technique that Pfahler follows is to make an anterior and a posterior plate before the injection of air in order to demonstrate the conditions present independent of the air injection. In this way one is able to localize the air or gases which may be retained in the rectum or pelvic colon. The urethral orifice is then cleansed in the usual manner and the largest catheter that is comfortable is passed into the bladder. An atomizer bulb is then attached to a glass connecting tube which in turn is connected to the catheter. After the bladder is emptied, it is distended with air by means of the atomizer bulb until the patient complains of discomfort. The catheter is then clamped and the pictures are taken, usually making one or more exposures posteriorly and the same number anteriorly. After the exposures have been made, the clamp is removed from the catheter and the air is allowed to flow from the bladder. Gentle pressure should be made in the suprapubic region in order to force all of the air from the bladder. Pfahler has never had any bad results from this method and he has frequently succeeded in demonstrating newgrowths in the bladder as small as a thimble.

Neo-Insertion of the Round Ligaments.—Every year brings forth its quota of round ligament operations for the purpose of suspending the uterus, many of which differ very slightly from methods already described. NICHOLSON (*Surg., Gynec. and Obst.*, 1919, xxiv, 194), of Buenos Ayres, now desires to bring to the attention of foreign surgeons the operation of "neo-insertion of the round ligaments" as perfected by Caballero which has given very satisfactory results in 1233 operations. It is employed only to correct fixed or irreducible retrodisplacements or in those cases in which some other abdominal condition, such as disease of the adnexa or appendix has made necessary a laparotomy, since in easily reduced retroversions he always employs the Alexander operation. The essential point in technique which the author describes is the making of a musculo-aponeurotic canal through which

the round ligament is drawn and then anchored to the rectus sheath. With a pair of Kocher forceps, the round ligament is seized about two inches from its uterine insertion, and another pair of Kocher forceps is introduced into the inferior portion of the wound, between the rectus muscle and its aponeurosis as far as the outer border of the rectal sheath and then is plunged through the sheath and peritoneum, entering the peritoneal cavity. This perforation occurs very near the internal orifice of the inguinal canal. The forceps are then opened and the round ligament is seized at the point where it was originally grasped by the first forceps. The forceps is then withdrawn bringing the round ligament with it and the ligament is sutured to the aponeurosis of the rectus about 5 millimeters from its border. The same procedure is performed on the opposite side and the abdomen is closed. This operation is very similar to the method of Simpson which is extensively practised in this country and the reviewer feels that Simpson's method is superior in that it is entirely extraperitoneal. The great argument against this type of operation is the possibility of injury to the deep epigastric artery but the author states that he cannot imagine how an artery the size of the epigastric could be injured by a blunt-pointed instrument. Up to the present time he does not know of a case of retrodisplacement that has recurred after this operation and he has had the opportunity of observing many patients who have been operated upon and who have become pregnant many times, the pregnancies terminating in normal labors. Among his cases there were several that were operated upon during the first few months of pregnancy and with one or two exceptions, the pregnancy has gone on to term and labor has been normal.

Bloodless Hysterectomy.—In order to overcome any possibility of secondary hemorrhage following the removal of the fundus uteri, VAN HOOSEN (*Surg., Gynec. and Obst.*, 1919, xxix, 196) has elaborated a technique whereby a bloodless hysterectomy may be performed. After the abdomen has been opened, the fundus of the uterus is grasped with a volsellum forceps and lifted well into the incision, or as high as possible. The assistant now maintains traction on the uterus while the operator places the index finger of the left hand under the round ligament and the thumb of the same hand under the ovarian ligament, at the same time retracting the broad ligament from the body of the uterus. With the right hand an 8-inch forceps (preferably of the angiotribe pattern) is placed on the body of the uterus from a point opposite the internal os to the tubal attachment and the forceps is closed slowly enough to allow the uterine musculature to slip to the inner side. The forceps is closed lightly without using the racquet. Another forceps is placed in similar manner internal to this and touching it throughout its length. The side opposite is treated in the same way. By this application of forceps the uterine artery and the uteroövarian anastomosis are pushed away from the body of the uterus and the peritoneum covering the uterus is rendered tense. The peritoneum over the uterus on both anterior and posterior surfaces is now incised, beginning one-half inch above the line where the peritoneum is intimately connected with the uterus and extending upward on each side parallel with the forceps and one-half inch internal to it. The peritoneum adjacent to the forceps on both the anterior and posterior surfaces is lifted by undercutting with a sharp knife. Strong traction is now made in turn

between the volsellum controlling and holding the body of the uterus and the forceps applied on each side and with a few strokes of the knife the uterine musculature is separated from the parametrium and the uterus is freed down to the internal os. With dissecting scissors the cervical musculature and mucosa is coned out for any distance, even to the external os if so desired, and lifted out with the attached body of the uterus. Neither ovarian nor uterine artery having been severed, the suturing may now be begun. The first suture is placed deeply uniting the anterior and posterior border of the cervical cone. The internal forceps on the edge of the severed broad ligaments are now removed and the remaining forceps are drawn together and held until the cut edges on each side can be united to each other with a lock stitch. The lateral edges are united first from the posterior surface and after removal of the remaining forceps from the anterior surface. If a generous border of peritoneum has been left there will be no surface uncovered by peritoneum except possibly at the tubal location. This can be better covered and at the same time the stump which represents a skeleton uterus can be elevated by passing a suture through each round ligament about one inch from the uterine attachment and by tying them together over the uterine skeleton and fixing them thereto. If the tubes are to be removed, an 8-inch angiotribe or strong forceps is placed on the broad ligament above the ovary and close to the tube and the tube is peeled out of its peritoneal covering and the cut edge of the peritoneum is ligated *en masse*, but not including the ovarian artery.

Stricture of the Ureter.—For several years HUNNER (*Southern Med. Jour.*, 1919, xii, 396) has devoted considerable time to the study of stricture of the ureter and his publications have been of much interest and value. In the study of about 500 cases of ureteral stricture occurring in his practice during the past four years he has arrived at a number of important conclusions. Some of these are startling because of their newness but none of them would have been presented had he not had full confidence that time and further investigation on the part of other men would give them support and verification. He believes that ureteral stricture is one of the commonest causes of abdominal symptoms in women. Unrecognized ureteral stricture leads to more needless and fruitless abdominal operations than any other pathological condition. These operations in the probable order of frequency are for appendicitis, ovarian disease, uterine and pelvic disorders, floating kidney, especially the type with hydronephrosis, gall-bladder investigations, and abdominal explorations for intestinal obstruction and adhesions. Ureteral stricture, according to Hunner, is the cause of more kidney pathology (excluding conditions usually classified as medical) than any one factor. It accounts for the majority of hydronephrosis cases, and thus indirectly for many cases of floating kidney and of pyonephrosis. The majority of pyelitis cases have ureteral stricture and obstruction as a basis. Most cases of pyelitis of pregnancy and of the puerperium depend upon stricture, as do many cases of pyelitis in children. Some cases of albuminuria and eclampsia leading to premature childbirth are due to stricture. Most cases of stone in the ureter and probably many cases of stone found in the kidney and bladder arise in an area of ureteral stricture. It is probable that urinary stasis due to stricture is the predisposing factor in many cases of stone arising in the kidney and of recurring

kidney stone after operation. Many, if not the majority of cases of so-called essential or idiopathic hematuria are due to ureteral stricture. Finally, Hunner states that time and experience have amply verified his original theory that most cases of ureteral stricture and many cases of chronic urethritis are due to focal infections. In order to arrive at an accurate diagnosis of this condition, a careful history must be taken in every case and this must be followed by a most painstaking physical examination. The urine analysis is then closely studied after which the newer methods of diagnosis are employed including roentgenography, cystoscopy and ureteral catheterization especially with the wax bulbed catheter.

Indications for Operation in Ureteral Calculi.—The discussion of the question whether or not to operate upon a case of ureteral calculus was a much easier task ten years ago than at the present time. This change in viewpoint is in great measure due to the rapid development of the non-operative methods of treatment, with which every surgeon should not only be familiar but give his patient the benefit of, before operation is considered. As a result of a rather extensive experience in renal surgery, EISENDRATH (*Ann. Surg.*, 1919, lxx, 192) has formulated some very helpful rules in determining the indications for operation. He believes that operation is indicated when colics recur or infection persists after repeated attempts have been made to deliver the calculus by non-operative methods and there is practically no change in the location of the calculus; also when there are evidences of stricture formation following (*a*) the spontaneous expulsion of a calculus, (*b*) or its delivery by non-operative methods, or (*c*) after a ureterotomy, or when a fistula is present either (*a*) as the result of perforation of the ureteral wall by a migrating calculus, or (*b*) above a stricture. Operation is certainly indicated when a severe degree of renal infection is present and the calculus is impacted in the ureter. Whether or not it is necessary to remove the kidney in addition to the ureterotomy depends on the degree of involvement of the renal pelvis and parenchyma. Some of these cases are complicated by a peri-ureteral or perinephritic abscess which will require immediate drainage. Calculous anuria cases should be operated upon as soon as the diagnosis of the location has been made. The average period of tolerance is six days. If the calculus is located near the vesical end of the ureter an attempt to deliver the calculus by manipulation is worthy of a single trial, but one should not lose valuable time by postponing operative interference too long while such an attempt is being made. In cases of either aseptic or infected hydronephrosis immediate operation is indicated. As a rule, the degree of dilatation of the renal pelvis is such that a nephrectomy is necessary. If pyelography can be done in such cases, it gives the best picture of the extent of the destruction of the parenchyma. Many of the cases in which an attempt has been made to save the kidney may be benefited by catheter drainage or renal pelvic lavage. Bilateral ureteral calculi alone without concomitant renal calculi occur so infrequently that it is best to consider the two together and in such cases the kidney with the acute complications should be operated on first. In cases where no complications are present, the kidney with the better function should be operated upon first although occasionally simultaneous bilateral operation is advisable.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
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Studies on Compensatory Hypertrophy of the Thyroid Gland.—The definition of conditions under which compensatory hypertrophy of the thyroid gland may be expected to occur, has been uncertain. LOEB (*Jour. Med. Res.*, 1919, xl, 199) presents his work on guinea-pigs. A particular description of the thyroid gland of guinea-pigs notes the normal variations in microscopic structure. Slight changes, indicating the beginning of hyperplasia are noted to occur following extirpation of one lobe, the removal of one-half lobe producing no demonstrable change. Definite hypertrophic changes were found after the extirpation of one lobe and about one-half to two-thirds of the other lobe. These changes were more marked after almost complete extirpation of both lobes; consisting of hypertrophy of the epithelial cells, diminution in colloid content with accompanying deformation of acini and an increase in the number of mitoses. The hypertrophy is apparently independent of age and only slightly influenced by general nutrition. In a majority of cases the hypertrophic changes occurred between the fifteenth and eighteenth days following operation and persisted for six to eight weeks. Pregnancy may occur after almost complete extirpation of both thyroids. In the major portion of cases abortion followed an almost complete extirpation of thyroid in the pregnant guinea-pig. Pregnancy does not usually interfere with the occurrence of compensatory hypertrophy. It may exert a slight inhibitory influence.

Microörganisms Found in Canned Foods.—The preservation of food by canning has been of interest from the medical bacteriological standpoint, because of the possibility of contamination by pathogenic organisms in such processes. CHENEY (*Jour. Med. Res.*, 1919, xl, 177) gives results of his work in the determination of whether viable organisms persist in apparently tight cans of merchantable foods, after modern sterilizing methods. The ordinary sources of contamination of foods before canning and the factors involved in spoilage of canned foods are reviewed. A brief survey is given of previous work on the problem directing attention to the types of organisms (principally non-pathogenic spore-bearers), previously found. There follows a detailed technic of obtaining cultures from the cans and their contents, and of the media used for identification of molds and yeasts, aërobes, anaërobes, gas forming and thermophilic bacteria. The percentage of cans containing living organisms in each kind of food was remarkably constant. The contamination seems to be in inverse proportion to the efficiency of the sterilization. A rather sharply limited group of

organisms was isolated, involving forms producing resistant spores, including the B. subtilis, mesentericus group, the related thermophiles, and one anaërobe. In addition four common species each of aspergillus and penicillium and two borderline yeasts were demonstrated. Seven hundred and twenty-five cases of merchantable food were examined for bacteria molds and yeasts. Eight per cent. of these cans were found to contain viable organisms, none of which were pathogenic. Vegetables constituted 8 per cent. of cans showing viable organisms, fruits 3 per cent., fish and meats 10 to 20 per cent. The contamination in fruits is principally moulds and in fish and meats bacteria.

Types of Streptococci Found in the Sputum of Bronchial Asthmatics.—WALKER and ATKINSON (*Jour. Med. Res.*, 1919, xl, 229) present the results of a study of fifty cases of bronchial asthma. Particular attention is given to the occurrence of streptococci which are typed according to Holman's classification, which they found a practical one. The technic of culturing and identifying the various strains is given in detail. Hemolytic streptococci were recovered from the sputum of 46 out of fifty patients, subacidus, anginosus, pyogenes and infrequens being the principal strains isolated. It is suggested that the protein of these four strains be used, in cutaneous tests on asthmatic patients. Evidence was offered that all of the types of hemolytic streptococci which were isolated, might become pathogenic. Of the non-hemolytic streptococci, non-hemolyticus I, ignavus, salivarius and mitis were most frequently isolated. The results of treatment of the fifty patients with autogenous sputum vaccines, consisting of the predominating organism are given. It is suggested that autogenous sputum vaccines be made at frequent intervals, because of the variation in the predominating organism. The washed sputum was found to be fairly free of mouth contamination and contained only eight distinct kinds of bacteria other than streptococci.

HYGIENE AND PUBLIC HEALTH

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Mental Deficiency of Prostitutes.—MERTZ (*Jour. Am. Med. Assn.*, 1919, lxxii, 1597) sums up the outstanding facts in the mental aspects of prostitution as found in Newport News as follows: (1) 53 per cent. of the women arrested for prostitution and kindred offences and held in the detention home for examination had a mental age

of ten or under; (2) in addition, 15 per cent. of those who were not mentally deficient showed mental disorder; (3) 10 per cent. were so deficient as to warrant, under existing laws, segregation in an institution for the feeble-minded; (4) 50 per cent. of these women did not reach the fifth grade in school; (5) if seeking for a "type," the composite of the delinquent woman as found in Newport News would seem to be a woman of nineteen, slightly mentally deficient, with schooling to the fourth grade.

The Effect of Freezing upon the Organisms of Typhoid Fever and Diphtheria.—An outbreak of diphtheria and one of typhoid fever which had been epidemiologically studied by officers of the United States Public Health Service, and seemed properly attributable to the ingestion of polluted ice-cream, prompted BOLTEN (*Pub. Health Rep.*, February 8, 1918) to institute experiments to determine how long the typhoid bacillus and the diphtheria bacterium could survive freezing and whether freezing had any influence upon the pathogenicity of the latter organism. To determine the resistance to freezing of the typhoid bacillus, he planted four metal containers of pasteurized cream, each with 5 c.c. of a twenty-four-hour broth culture of Bacillus typhosus (Rawling's), froze them in a brine tank and on each successive day for about a month, and on every alternate day for about another month, melted and refroze them after streaking a loopful from each container across an Endo plate. During the first few days there was very little change in the number of colonies per plate, but after ten days to two weeks only about half the number were counted as compared with the original plate counts. At the end of the month the colonies developed were very few, about one-twentieth of the number on the original plates. Finally the containers were kept frozen continuously for eighteen days and again tested. In two of the containers the cultures were apparently killed, since no growth was obtained on the Endo plates; the other two containers continued to show slight growth, one colony per loop from one and six from the other. To study the effect of freezing upon the viability and toxin production of Bacterium diphtheriæ, eight pure cultures, isolated from clinical cases during the epidemic, were used. Two small Loeffler slant tubes were planted respectively with each culture and incubated for twenty-four hours at 37° C. One of these was harvested with 5 c.c. of salt solution and added to 40 c.c. of pasteurized cream. These cultures were frozen for four days, when subcultures were made in 2 per cent. neutral peptone from the frozen cultures and the unfrozen controls. The subcultures were incubated for five days at 37° C. On the fifth day guinea-pigs were inoculated with 1 c.c. of each of the broth cultures, eight pigs for the frozen and eight pigs for the unfrozen cultures. On the basis of this experimental work the conclusion was drawn that ice-cream may be regarded as a possible agent in the distribution of typhoid fever and diphtheria.

Detection of Bacillus Tetani in Vaccine Virus.—The appearance of a number of cases of tetanus in a community following a more or less general vaccination against smallpox raised the suspicion of tetanus contamination of the vaccine virus used, and made necessary an attempt to determine the source of contamination. McCOY and

BENGSTON (*Hyg. Lab. Bull.*, No. 115) report the results of a systematic bacteriological investigation and emphasize the salient facts established. From the history of the cases of developed tetanus it was shown that the vaccinations against smallpox had been practised exclusively with ivory points from a single manufacturer. After taking administrative action to prevent further distribution of the suspected vaccine material and to effect the recall of that already on the market the investigation was begun. First, uncharged ivory points, just as they were received from the manufacturer of ivory points by the manufacturer of the vaccine, were examined by planting them under anaërobic conditions, with the result that tetanus-like organisms developed in some of these cultures and animal inoculations (guinea-pigs and mice) with the contents of these tubes demonstrated the presence of tetanus spores on uncharged ivory points. The next step was to determine if this tetanus contamination is common with the ivory point of other manufacturers. The ivory points of three different manufacturers were tested in the same way, with the result that tetanus organisms were detected on the points furnished by two establishments. It is the practice of the manufacturers of vaccine points to "sterilize" the ivory points before charging them with the vaccine material. A large number of ivory points that had been "sterilized" and made ready for charging with vaccine material by the manufacturer whose vaccine points were under suspicion were examined, with the result that tetanus spores were detected in several. Tests were made of fourteen different laboratory numbers of packages of vaccine points from the manufacturer under suspicion, with the result that in four flasks, all of which had been planted with points of the same laboratory number, tetanus organisms were detected by mice inoculation. Capillary tubes of vaccine virus of the same suspected manufacturer showed no growths. The same negative results were obtained with plantings of glycerinated lymph and bulk vaccine of this manufacturer. Supplemental experimental work was carried out to determine the conditions most favorable for the growth of Bacillus tetani and the formation of tetanus toxin in contaminated vaccine virus.

The Physician's Responsibility in Diphtheria.—In a study of 1000 deaths from diphtheria made by Dr. B. W. CAREY, of the Massachusetts State Department of Health (*Boston Med. and Surg. Jour.*, January 16, 1919), evidence is presented which shows that for various reasons the abundant fund of useful knowledge which medical science has at its disposal for dealing with diphtheria is still utilized far too little. Especially discouraging, after the many years of exhortation to call a doctor at once, is the fact that in over 23 per cent. of the cases the patients had been ill a week before the physician was called. In 4.2 per cent. the patients had been ill from one to two weeks before they received medical attention. It is also surprising to find that in a populous State like Massachusetts, where laboratory facilities as well as antitoxin and Schick outfits are conveniently available, 7.6 per cent. of the deaths should have occurred in "unrecognized" cases. Apparently this denotes carelessness on the part of the medical profession. It is certain, as the Massachusetts State Health authorities point out, that health authorities have a right to expect that the diagnostic and therapeutic facilities which they furnish be utilized by the practising physicians to

effect a diminution of the morbidity and mortality of diphtheria. Inquiries as to the dosage and use of diphtheria antitoxin also indicated that physicians were not utilizing this remedy in accordance with the best experience. In a number of fatal cases studied the physician had delayed antitoxin treatment by waiting for a laboratory confirmation of the diagnosis. In not a single instance was the antitoxin given intravenously, and this despite the fact that in several cases antitoxin was administered every four hours until death occurred, in one instance a total of 80,000 units being given this way. That the complaint of the Massachusetts State health authorities is not only well justified, but that it probably voices a legitimate indictment of a part of the medical profession generally, is indicated by the fact that a very similar complaint was made by the New York City health authorities a year or two ago. With a diagnostic laboratory service unsurpassed, and with Schick test outfits, antitoxin serum, and active immunization outfits practically at their elbow, the physicians of New York were charged with insufficient or delayed utilization of these aids and with responsibility in the continued prevalence of fatal cases of diphtheria. It is possible that a thorough investigation of every fatal case of diphtheria, with a request for an explanation by the attending physician, might serve to make those who are now negligent in their management of cases of diphtheria exercise greater care and thus lead to a saving of life.

Preliminary Report on Carbon Tetrachloride Vapor as a Delousing Agent.—Foster (*U. S. Public Health Reports*, October 25, 1918, states that the effectiveness of dry and moist heat and hydrocyanic acid gas as a means of destroying body lice on clothing has been thoroughly investigated. These processes, while effective, require the use of a somewhat complicated apparatus which is not easily transported and not always available for troops in actual warfare. Also in civilian life the problem of cleaning up lousy clothing without special appliances occasionally presents itself in jails, small hospitals, asylums, camps and even the home. In the search for some practical method of destroying lice which could be applied with simple apparatus and which would not injure woollen fabrics the writer was led to investigate the effects of carbon tetrachloride vapor. The vapor of carbon tetrachloride was contrasted with that of gasoline and chloroform in regard to its effect on flies and was found to be much more toxic to these insects than either of the other two. The pure vapor killed unprotected lice in fifteen minutes but failed to destroy them in ten minutes. The following method was thoroughly tested: A 10-gallon tin can, such as is used for shipping liquid disinfectants, was obtained. The top was cut out so that clothing could be introduced and removed readily. The complete outfit of wearing apparel was placed in the tin and pressed down rather firmly, occupying a little more than one-half of the total space. Several layers of filter paper were laid on top of the clothing, and on this paper 25 c.c. of carbon tetrachloride was poured. The top of the can was covered by several thicknesses of towelling and a loose cover placed over this, the idea being to protect the can from the effects of drafts but not to seal it hermetically, so as to permit some of the air to escape at the top when it was displaced at the bottom by the heavy vapor. At the end of two hours the can was opened and the package containing

the lice-infested shirt was aired and examined. All the lice were found to be dead, and they did not revive when examined at various periods up to twenty-four hours afterward. It was ascertained that exposure, under similar conditions, to the same strength of carbon tetrachloride for an hour and a half was not sufficient to kill all the lice, about 25 per cent. surviving. It was also found that a lesser amount of carbon tetrachloride was not sufficient to kill the lice in two hours. These experiments were repeated in various ways with lice, on pieces of cloth contained in test-tubes at both ends, but fairly tightly sealed with cotton plugs. These tubes were tightly wrapped in all the various articles of clothing, and it was found that 25 c.c. of carbon tetrachloride, with exposure of two hours, was sufficient to kill all the lice. The garments were hung up and aired for an hour, after which no odor of carbon tetrachloride could be detected on them. The fact that carbon tetrachloride is the base of one of the widely advertised cleaning fluids for removing grease spots from clothing would seem to indicate that its use in the hands of the laity is not accompanied by any grave danger. It is not contemplated to propose it as a substitute for the heat of cyanide gas treatments where these are available, as they would certainly be much more economical where large bodies of men are to be deloused at one time and in one place.

Disabling Sickness in Relation to Family Income.—SYDENSTRUCKER, WHEELER and GOLDBERGER (*Public Health Reports*, November 28, 1918), state that the experience derived from the census of sickness and from the records of working days lost on account of sickness in the seven cotton mill villages studied appears to suggest the following: A higher sickness (involving inability to work) rate and a greater amount of working time lost on account of such sickness were found among members of families whose incomes were at a low status. This condition appeared for persons of either sex and of similar ages. Only when a family income approximated $10 per half month per adult male unit (or about $900 a year for a family of "normal" size in 1916) did the sickness rate appear to be as low as that suggested by similar censuses in a number of localities in the United States as the normal rate. Low economic status appeared to be a more striking concomitant of high sickness rate among females than employment in mill work. A greater proportion of disabling illness, of relatively long duration, appeared among persons whose family income was below the average than among persons with a more favorable economic status. To what extent low family income was a cause of higher sickness rate and to what extent it was an effect of disability (and thus of inability to increase income) cannot be determined. The condition, however, is manifest that a greater amount of disabling sickness existed among persons who were living under less favorable economic conditions than among persons whose economic status was more favorable—a condition which has been pointed out by previous observations in literature on the social aspects of ill health and indicated by several recent studies. The data here presented afford additional ground for the suggestion that in the analysis of morbidity facts the factor of economic status should be given proper emphasis.

Typhoid Fever and Municipal Administration.—FREEMAN (*Public Health Reports*, 1918. xxxii, 643) presents a study of the means of typhoid fever prevention employed in its relation to the prevalence of the disease in a group of cities in the Ohio River Valley. The conclusions drawn from a study of the means employed are strikingly borne out by the prevalence of typhoid fever in the group of cities included. The major factors in typhoid fever causation—polluted water and improper disposal of human excreta—are still largely operative. The minor factors, with the exception of the pasteurization of milk, are largely ignored. The group of cities, fairly representative of a very large class of American municipalities, still suffers from an excessive prevalence of typhoid fever, due to well-understood and easily preventable causes.

Trinitritoluene Poisoning.—An extensive investigation of trinitritoluene poisoning by VOEGTLIN, HOOPER and JOHNSON (*Public Health Reports*, 1919, xxxiv, 1307) gave results which may be summarized as follows: A great difference in susceptibility of various animals was found; dogs (and probably men) are much more susceptible than are white rats, guinea-pigs and rabbits. The symptoms in dogs are cyanosis, diarrhea, salivation, incoördination, icterus and anemia, sometimes with loss of weight. The chemical is absorbed through the skin, through the gastrointestinal, the respiratory tract and from the subcutaneous tissue. The urine shows a positive Webster test early, but the reaction is not due to T. N. T. but to a metabolic product of the latter. The feces never give this test. The minimum toxic dose is less than 5 mg. per kilo and no tolerance is established. The highly purified T. N. T. is just as poisonous as is the commercial product—in other words, the poisoning is not due to impurities of the product. In chronic cases anemia of varying intensity develops. A varnish made of shellac, castor oil and alcohol is suggested for application to the hands and the forearms as a prophylactic agent, and cotton gloves impregnated with a modification of this varnish are also suggested. Sodium hydrosulphite and sodium sulphite are excellent solutions for removing the poison from the skin. It is recommended that a fall of hemoglobin of 15 per cent. to 20 per cent. be regarded as an indication for taking an individual off work which exposes him to T. N. T., and the appearance of bile pigments in the urine should be dealt with in the same way. A generous diet, particularly one rich in meat, the elimination of susceptible workers, free ventilation of factories, and the use of the gloves or varnish are the chief means of dealing with T. N. T. industrial poisoning.

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